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WARDROP GRIFFITH (in uniform) and THOMAS LEWIS during the 1914–18 war.

Photo by John Hay

THOMAS WARDROP GRIFFITH

Professor Wardrop Griffith can only have been known personally to few members of the British Cardiac Society, as it is sixty years since he became Professor of Anatomy in the Yorkshire Medical School at Leeds: and he flourished as a physician in the generation between those of Clifford Allbutt and of the present most senior physicians in Leeds.

Wardrop Griffith was born in 1861, the tenth child and eighth son of Charles Fox Griffith, J.P., of Aberdeen. He was educated at the Aberdeen Grammar School, and the University of Aberdeen, where he qualified in April 1882 with the highest honours. After qualification he acted as demonstrator in anatomy to John Struthers for four terms, and under that master got a thorough training in dissecting-room anatomy.

In October 1883 he took the post of house physician at Leeds General Infirmary, and the next year was appointed the resident medical officer. This post he retained until his appointment as Professor of Anatomy in the Yorkshire College in Leeds in 1887. As this was a part-time Chair, Griffith put up his plate in Park Square, and started practice as a physician. In 1892, in addition to his professorship of anatomy, he was appointed an honorary assistant physician at the Leeds General Infirmary. In 1904 he was elected physician in charge of outpatients, and became a full honorary physician in 1905, from which post he retired in 1925. He held the Professorship of Anatomy up to the year 1910, when he became Professor of Medicine; he resigned the chair in 1925, when he retired from the Leeds Infirmary.

Wardrop Griffith made a great reputation as a teacher of anatomy. Despite the fact that he obtained the chair at the early age of 26 years and also that it was a part-time post, he took the School of Anatomy at Leeds to the front rank, both by the thoroughness of his work and his brilliance as a lecturer. As pointed out by an old student in the Yorkshire Post on October 29, 1946, " He was a pupil of the great John Struthers, and inherited from him an exact and lucid conception of anatomy, and a great power of elucidating much of its mysteries. He was a man who impressed students, and no student ever played the fool at his lectures. His presence in the dissecting room was always welcome, and his demonstrating powers were of a high order." He had examined in Anatomy in the Natural Science Tripos and the 2nd M.B. examination at Cambridge.

There was something of the dramatic in Griffith's teaching, of which those of us who heard him talk in the Cardiac Society and at the Association of Physicians were well aware. In his anatomical lectures he was wont to jump on to a table to illustrate the action of muscles and joints, and was wont to perform other acts of pantomime. His students, when they came together in after years, took pleasure in recalling their memories of Wardrop Griffith, chiefly as a teacher of anatomy with his little mannerisms, his punctuality, and his kindliness.

While holding the Chair of Medicine, his lectures were equally lucid and thorough, and his teaching at the Infirmary was very sound, but it is doubtful whether he ever produced quite the same atmosphere as obtained at his lectures in anatomy. Griffith was extremely assiduous and punctual in all his hospital and university duties, and expected punctuality from others as well. He identified himself very closely with the Leeds Medical School, and so great was his share in this, that it was said that, " he personally supervised the laying of every brick." As Dr. Veale stated, while presenting Griffith for the Honorary D.Sc. in 1929, " There is little over-statement in this, for the University owes him a lasting debt of gratitude for the careful planning and sound construction of this building, which now, though being substantially enlarged, still remains a lasting memorial of his efforts."

In the clinical school he founded the clinic for diseases of the skin, and was one of the first to make use of the graphic methods of cardiovascular investigation suggested by the work of James Mackenzie and Thomas Lewis.

Wardrop Griffith was one of the original members of the Cardiac Club when it was founded in 1922, and in the early years was very regular in his attendance, and could always be relied upon to give an authoritative opinion on any anatomical question. In 1924 he opened a discussion on the heart in pneumonia. He was, however, already getting senior and most of his active writing had already been done so that he was elected an Extra-Ordinary Member as long ago as 1928. In the third volume of *Heart* he published an exhaustive paper on two cases of heart block, in which he noted the ausculatory phenomenon of auricular beats. He gave the Schorstein lecture on some cardiac problems in 1912. He was a critical worker and Thomas Lewis gave much importance to his opinion, and often submitted work for his criticism. In Griffith's home circle, " Thomas Lewis " became a family saying, meaning he was thinking about something else!

Griffith had taken the M.R.C.P. in 1901 and was elected F.R.C.P. in 1908. He served on the Council of the Royal College of Physicians from 1924 to 1926. He acted as examiner in Medicine in the Universities of Cambridge and Manchester. In 1922 his own University of Aberdeen conferred upon him its Doctorate of Law, and Leeds University conferred upon him the Honorary Degree of Doctor of Science.

Tall, well proportioned, and good looking, there was a certain charm of manner in Wardrop Griffith, which made him very approachable to younger members of the profession, and he was a real friend to all the early members of the Cardiac Club, and was intensely interested in any work that any of them were doing. His memory was prodigious, and he could reel off pages of poetry chiefly of the lighter kind such as Gilbert and Sullivan, Bab Ballads, etc. He was an authority on the Waverley novels, and knew the stories and characters well. He had also the same intimate knowledge of Dickens and Thackeray.

During the War of 1914–18, Wardrop Griffith served with Number 2 Northern General Hospital at Beckett's Park, Leeds, and in 1918 was appointed C.M.G. From 1918–27, he represented the University of Leeds on the General Medical Council.

Being one of ten children, he always kept in touch with the remaining brothers and their children: his two sisters died fairly early in life. The evening of Wardrop Griffith's life was saddened by the loss of his wife in 1937, and the gradual loss of his eyesight, so that he was unable to read for the last three years.

We mourn the loss of our most senior member, whose youthful outlook on medicine kept him in touch and sympathy with his junior colleagues long after he had retired from the active staff of the Leeds Infirmary, at a time when his great clinical experience and critical outlook was most helpful.

W. E. HUME

Thirteen years ago, when I attended the meeting of the Cardiac Club at Leeds, I have a clear memory of Wardrop Griffith: of the distinguished way he presided over the meeting, of his lucid demonstration of specimens of congenital heart disease, and of his kindness to me a very junior member of the Club. It has, therefore, been a great pleasure with the help of John Towers, compiling this bibliography of his publications on cardiology. His first paper, in 1889, written for his M.D. thesis, was on 50 cases of empyema, but very soon he had started his interest in congenital heart disease. His remaining papers dealt mainly with other anatomical abnormalities and with nervous diseases.

MAURICE CAMPBELL

Remarks on fifty consecutive cases of empyema occurring in the medical wards of the general infirmary at Leeds. *Med. Chron.* (1888–9), **9**, 441.

A case of transposition of the thoracic and abdominal viscera, with congenital malformation of the heart and of the arterial and venous systems. *J. Anat. & Physiol.* (1891–2), **26**, 117.

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Example of a large opening between the two auricles of the heart unconnected with the fossa ovalis. *J. Anat. & Physiol.* (1899), **33**, 261.

Obstruction of the inferior vena cava. *J. Anat. & Physiol.* (1899), **33**, 503.

Specimen of great redundancy of the fossa ovalis. *J. Anat. & Physiol.* (1899), **33**, 502.

Two examples of moderator band in the left ventricle of the heart. *J. Anat. & Physiol.* (1899), **33**, 31.

Remarks on aneurysm of the coronary arteries of the heart. *Brit. Med. J.* (1931), **1**, 266.

Abnormalities of the heart. *J. Anat. & Physiol.* (1902), **36**, 26.

A case of almost complete absence of the auricular septum and other cardiac malformations complicated by acquired mitral disease. *Med. Chron.* (1903), **37**, 385.

An example of a peculiar malformation of the tricuspid valve of the heart. *J. Anat. & Physiol.* (1903), **38**, 251.

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Infective endocarditis involving the pulmonary valves and associated with imperfection of the inter-auricular septum. *Lancet* (1906), **11**, 973.

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(with A. M. Kennedy): A case of complete auriculo-ventricular heart block with a report of the pathological condition of the heart. *Brit. Med. J.* (1913), **1**, 1203.

A presidential address on the development of our knowledge of the diseases of the heart. *Lancet* (1913), **11**, 1517.

(with A. M. Kennedy): Supplementary note on a case of heart block; with an examination of the auriculo-ventricular junctional tissue. *Heart* (1914–15), **6**, 37.

Remarks on a communication between the two ventricles of the heart occupying an unusual situation. *Lancet* (1915), **1**, 59.

Two cases of patency of the ductus arteriosus. *Quart. J. Med.* (1915), **8**, 191.

Embolic aneurysm of peripheral arteries. *Lancet* (1920), **11**, 374.

A clinical study of three cases of heart block. *Brit. Med. J.* (1921), **1**, 763, and 956.

(with J. Hay *et al.*): Discussion on cardiac irregularities: especially in reference to prognosis and treatment. *Brit. Med. J.* (1924), **11**, 697.

CHARLES HERAPATH

Charles E. K. Herapath was born in Bristol in 1882, and was the son of a well-known and beloved general practitioner. He was educated at Clifton, at University College, Bristol, and at the Bristol Royal Infirmary. After qualifying M.B., B.S., in 1907, he held various house appointments and completed his studies in London, taking the M.D. in 1910. On returning to Bristol he was appointed to the staff of the Bristol Dispensary but maintained his connections with the Royal Infirmary. He joined the Territorials and became one of the keenest and most efficient officers in his unit. He enjoyed the army drill and discipline and was almost an authority on army regulations which appealed to his precise and accurate mind. During the 1914–18 war he served throughout as a company medical officer, was awarded the M.C., and earned the lasting esteem of his men.

On his return from war service he was appointed Assistant Physician, and later Physician, to the Bristol Royal Infirmary and here he developed his interest and enthusiasm in cardiology. His attraction in this branch of medicine was probably partly due to his love of mechanical " gadgets " and the consequent appeal of Mackenzie's polygraph. It was the same mechanical bent that made him an enthusiastic motor cyclist at a time when every expedition on a motor cycle was something of an adventure. As a result of his early work with the polygraph one of his main interests in cardiology was the study of the arrhythmias and his long records of patients with heart block and Stokes-Adams syndrome will be remembered. He was probably never happier than when struggling to correct some minor defect in his electrocardiograph or puzzling out some obscure cardiac arrhythmia.

Herapath was elected a member of the Cardiac Club in 1924 when it met at Bristol under the chairmanship of Carey Coombs. He attended the meetings regularly but did not give many communications, though in 1932 he was asked to open the discussion on the heart in influenza.

Apart from cardiology his other great interests were freemasonry, stamp-collecting, and music. The advent of wireless and the consequent possibility of listening to first-class music in the comfort of his own home was a great delight to him. Herapath was supremely happy in his home and marriage; but he was a rather shy man and not one who made friends readily, and as a result had few intimate companions. However, once the superficial reserve was penetrated it would be impossible to find a more loyal or staunch friend.

During the last years of his life he looked forward to retiring to a small house in the country, and it was a great tragedy that his death should occur so shortly after he acquired a house and garden at Keynsham, in which he was taking such a great delight.

He leaves a widow, one daughter, and one son who is, at present, a medical student.

C. BRUCE PERRY

Auricular fibrillation. *Bristol med.-chir. J.* (1911), **29**, 148.

(with H. Waldo): A case of complete heart block, with post-mortem examination. *Lancet* (1922), **1**, 271.

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PAROXYSMAL TACHYCARDIA FOLLOWED BY TEMPORARY INVERSION OF THE T WAVES

BY

R. E. STEEN

From the Meath Hospital, Dublin

Received March 1, 1947

It is now generally recognized that inversion of T waves such as is met with in coronary disease can occur in a number of other conditions also, for example, in myocardial disease due to toxæmia or hypertension, from large doses of digitalis, from the physiological effects of taking cold drinks, as a result of the position of the heart, and even from changes of posture especially in persons of the neuro-circulatory asthenic type.

Attention has, however, only recently been given in the literature to the fact that electrocardiographic features simulating serious coronary disease may in certain cases occur as a transient feature after paroxysmal tachycardia. The condition, furthermore, is of more than mere academic importance, since if not recognized, an erroneous diagnosis of coronary disease may easily be made especially if the attack of paroxysmal tachycardia passes unnoticed or is thought to have been an acute coronary lesion. Either these changes after paroxysmal tachycardia are very rare or it would seem possible that cardiologists have been familiar with their occurrence but have not recorded them.

White *et al.* (1941) in a review of various conditions other than organic disease causing inversion of the T wave in lead II makes no mention of paroxysmal tachycardia, and in a search of British and American papers only eighteen previous cases appear to have been described. Graybiel and White (1934) reported two cases of paroxysmal ventricular tachycardia in young robust adults, one followed by inverted T I and the other by inverted T II and T III; there was no sign of organic disease, and there was a gradual return to a normal cardiogram. Campbell and Elliott (1939) described two cases of paroxysmal tachycardia, one being ventricular, that gave transient changes simulating coronary thrombosis: one of these gave a history of diphtheria, and the other was of long standing and had been suffering from increasing dyspnœa during the intervals between attacks; both died at a later date. Though these two cases differ in their organic nature from the other cases described and from the present one, which except for the electrocardiographic abnormality seemed normal in other respects, Campbell and Elliott nevertheless laid stress on the transient nature of the cardiographic changes following the tachycardia. Cossio, Sabathie, and Berconsky (1941) described four cases, and Campbell (1942) a further three cases that were clinically benign. Currie (1942) described a further case probably of ventricular origin in a girl aged thirteen, followed by inversion of T waves, and a return to a normal cardiogram in one month. Dubbs and Parmet (1942) added a further case, Geiger (1943) one case, Zimmerman (1944) three cases, and Ward (1946) one case. The present case was one of paroxysmal auricular tachycardia and was clinically benign.

Present Case

A woman, aged 27, was admitted to the Meath Hospital, Dublin, on February 16, 1945. The history was that quite suddenly when she was walking three days previously her heart began to beat very heavily and she found her breathing became difficult. She also felt inclined

to vomit but was unable to, and experienced a throbbing sensation in her throat. She stated that she had a similar attack but milder in character a year previously. There was nothing of importance in the family history. Physical examination was normal except for some bad teeth, the rapid heart action, and a suspicion of œdema in her legs. The heart rate was extremely rapid and regular so that it was impossible to estimate the rate of the pulse at the

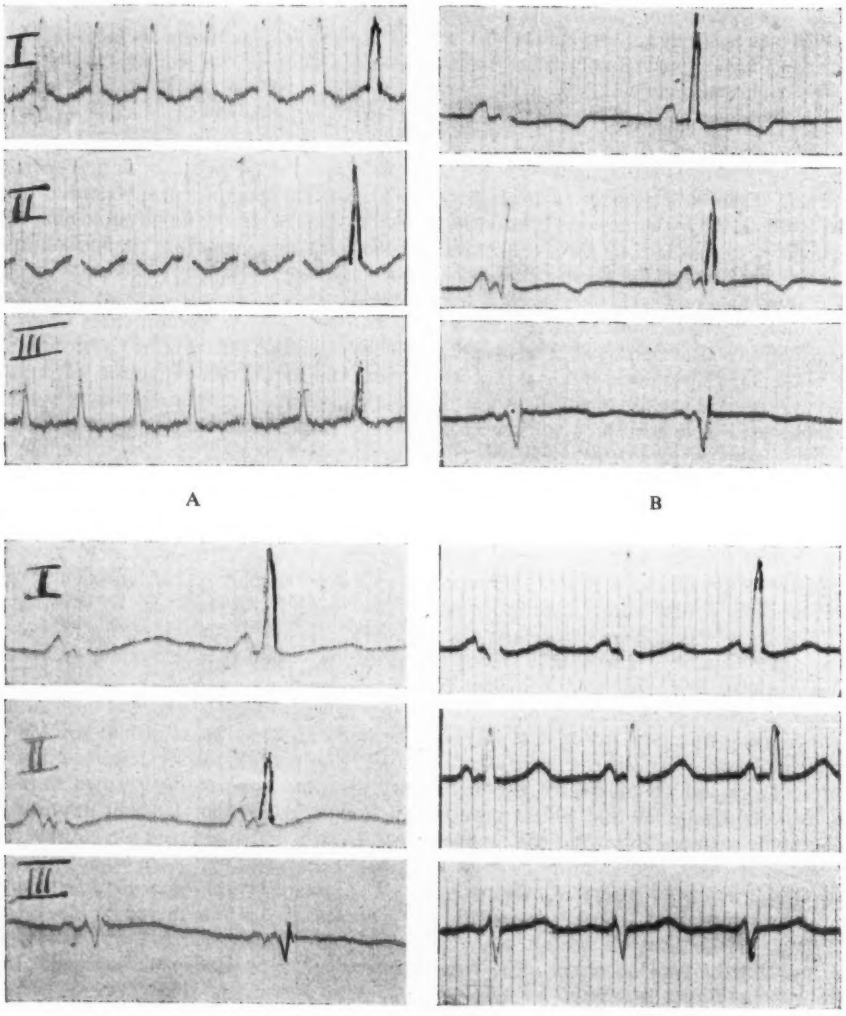

FIG. 1.—(A) Paroxysmal auricular tachycardia (16/2/45). (B) Inversion of T I and T II six days after cessation of attack (24/2/45). (C) More normal appearance of T I and T II two days later (26/2/45). (D) Completely normal T I and T II sixteen months later (20/6/46). In each case one complex has been inked in to mark it more clearly.

wrist, but when taken at the apex beat by auscultation it was found to be approximately 240 a minute, a figure that actually agreed with the rate as timed on the electrocardiogram. The method of tapping with the foot synchronously with the sound as heard on auscultation advised by Levine for timing cases of rapid heart action was found helpful in this case as otherwise it would have been very difficult to time at all accurately the extremely rapid heart rate.

Attempts to control the rapid heart action by the ordinary simpler methods were unsuccessful but the attack finally stopped between 7 a.m. and 1 p.m. on the morning of February 18, 1945, after 24 grains of quinidine sulphate had been given, spread over a period of 36 hours, the attack having lasted in all approximately four-and-a-half days. All other investigations both cardiological and otherwise were negative, including the Wassermann reaction.

Subsequent convalescence was uneventful except that the patient complained that she had a very slight attack on February 26 which she stopped herself by ocular pressure. The patient was discharged on March 21, 1945.

The electrocardiograms demonstrate the transient occurrence of inversion of T waves in leads I and II. Fig. 1A on February 16, the day of admission, shows typical paroxysmal auricular tachycardia. Fig. 1B on February 24, six days after the cessation of the attack, shows typical inversion of T I and T II. Fig. 1C taken on February 26, two days later, shows the T waves no longer inverted. Fig. 1D on June 20, 1946, sixteen months later when the patient felt perfectly healthy except that she was pregnant at the time, shows a normal cardiogram.

Discussion

The importance of not confusing a benign condition like the above with serious cardiac disease has already been stressed. It is of interest to consider the possible ætiological factors that may play a part in producing the abnormal electrocardiographic findings. Clearly even if the condition is less rare than it would seem, only a small minority of cases of paroxysmal tachycardia are associated with the abnormal type of cardiogram. Campbell suggests two possible explanations (1) " chemical or other changes in the myocardium as a result of a prolonged attack " and adds that " in this sense the changes would, to some extent, be a measure as to the severity and seriousness of the attack, and might indicate the need for adequate rest " or (2) " that it depends on changes in the position of the heart, and that as the diaphragm sinks, or as the stomach empties, the heart returns to its more normal position with the return to its normal electrocardiographic pattern." While he mentions in support of this view that it would bring the case into line with some of the other T wave changes reported from alterations in the position of the heart, he is inclined to discount this latter theory from the fact that the time taken for recovery from the electrocardiographic changes is measured in days rather than in hours. He sums up his views by saying that the condition " does not indicate any organic disease, but is a completely reversible process indicating some degree of exhaustion or strain of the heart muscle." The title of his paper " Inversion of T waves after long paroxysms of tachycardia " suggests that one of the most dominant factors is the length of the attack, and Currie also refers to this causative factor in support of which was the fact that in his case the changes in the cardiogram were less in an attack of short duration compared with one of longer duration. In the present case the attack lasted probably between four and five days and duration may have been a factor in the changes, but it is also worth noting that the rate of 240 a minute is an exceptionally high one, and since rapid heart action is well-recognized as a strain on the heart, it is possible that in this case the high rate of striking may have played an important part in determining the cardiographic changes. That such changes should occur is not surprising when one remembers that pulsus alternans and anginal pain are quite commonly experienced in paroxysmal tachycardia of

benign type, and that inversion of the T wave in lead I is considered as the cardiographic equivalent of pulsus alternans in cases of coronary disease.

From the practical point of view it is hoped that by the recording of this and other cases, otherwise healthy people may be prevented from being condemned to a life of cardiac invalidism.

Summary

A case of paroxysmal tachycardia with temporary inversion of T waves in leads I and II is reported. This brings the total number of such cases published in British and American journals to nineteen. Stress is laid on the possible influence of the very high rate of tachycardia in this particular case as an ætiological factor in the electrocardiographic changes. The ease with which these changes may be confused with coronary disease is emphasized.

I am indebted to Dr. P. T. O'Farrell of St. Vincent's Hospital, Dublin, for drawing my attention to the rarity of the present case, for help with the literature on the subject, and for kindly criticism and advice.

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THE EFFECT OF DEMEROL, ERGOTAMINE, AND DIHYDRO-ERGOTAMINE ON MORTALITY AFTER CORONARY OCCLUSION IN DOGS

BY

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In a previous report (Manning *et al.*, 1939) it was shown that fatal ventricular fibrillation occurred in 75 per cent of untreated conscious dogs following sudden occlusion of the left circumflex branch of the left coronary artery. This mortality can be reduced to 10 per cent by bilateral sympathetic denervation of the heart before ligation (McEachern *et al.*, 1940). It has also been shown that coronary dilator and anti-spasmodic drugs are effective, but to a lesser degree, in reducing this mortality (McEachern *et al.*, 1941; Le Roy *et al.*, 1941, 1942; Gilbert, 1942). These results have been confirmed by Gilbert and his associates whose further work supported the suggestion that a reflex coronary spasm initiated by the occlusion resulted in a generalized myocardial ischæmia which led to the fatal sequence of events (McEachern *et al.*, 1940; Le Roy *et al.*, 1941, 1942; Gilbert, 1942). It was also pointed out that sympathetic denervation may have rendered the myocardium less susceptible to the onset of ventricular tachycardia and fibrillation initiated by the infarction, rather than by interruption of a reflex arc (McEachern *et al.*, 1940). Possibly, both types of mechanism were present.

In view of these findings and the work of others (Leriche *et al.*, 1931; Miller, 1939; Evans, 1940; Katz and Joachim, 1939, 1945; Falk, 1942; Gregg and Shipley, 1944, 1945; Orth, 1946; and Harris, 1946), it was considered advisable to investigate the effect of sympathetic inhibiting agents, using the same experimental conditions and procedure previously described (Manning *et al.*, 1939). For this purpose ergotamine tartrate (Gynergen II, Sandoz) was used and also a new ergot derivative, dihydro-ergotamine (DHE-45, Sandoz).

Stoll and Hoffman (1943) have prepared a crystalline alkaloid derivative by hydrogenation of ergotamine which is less toxic and exerts a sympathetic inhibiting action stronger than ergotamine (Rothlin and Brügger, 1945). Dihydro-ergotamine lowers the blood pressure and slows the heart rate in the narcotized cat and rabbit. It is reported that DHE-45 acts on effector organs in such a way as to render them indifferent to sympathetic impulses.

Orth (1946) found that 0·4 mg./kilo. prevented cyclo-propane-epinephrine induced ventricular fibrillation in the dog. Using rats it was demonstrated that the oxytocic effects did not occur. Gangrene in the rat's tail was rarely produced following large injections of DHE-45 for more than thirty days. The dose recommended by Orth is approximately twice the dose of ergotamine tartrate for the prevention of cardiac effects due to cyclopropane and epinephrine. The protection lasted for about one hour and the epinephrine reversal of blood pressure in anæsthetized dogs did not occur.

Clinical reports have indicated that DHE-45, in doses of 1 mg. intramuscularly, is as effective as ergotamine tartrate in the relief of migraine (Horton *et al.*, 1945). It did not produce the disturbing side effects of other ergot preparations and in this dosage it had no demonstrable effect on the uterus, heart rate, blood pressure, peripheral arterial pulsation, or on the temperature and colour of the extremities (Horton *et al.*, 1945; and Hartmann, 1945).

In view of the results previously obtained (McEachern *et al.*, 1940; Le Roy *et al.*, 1941, 1942; Gilbert, 1942; Falk, 1942; Swanson, 1945; Mokotoff and Katz, 1945; Gerger, 1945; and Lindner and Katz, 1941) with coronary dilator or antispasmodic drugs, it was considered advisable to include in this study a small series of experiments with demerol. The hydrochloride of the ethyl ester of methyl-4-phenylpiperidine-4-carboxylic acid (demerol), discovered in 1939 in Germany (Gruber *et al.*, 1941; and Hori and Gold, 1944), is said to possess antispasmotic or parasympathetic-depressent, analgesic, and sedative effects and has been used clinically for this purpose with some degree of success (Hori and Gold, 1944; and Flatt, 1946).

Methods

Seventy-two normal dogs were used in these experiments. At operation a loose ligature was placed around the left circumflex branch of the left coronary artery close to its origin as described in a previous report (Manning *et al.*, 1939). The free ends of the loose ligature were brought out of the chest at either end of the skin incision and the chest closed in layers. A sterile dressing protected both the skin incision and the free ends of the ligature. The following day (24 hours later) ligation was effected by traction on the loose ends of the ligature.

Three groups of experiments were carried out using demerol, ergotamine tartrate, and dihydro-ergotamine. In addition, 8 dogs were ligated without the use of drugs, as a check on our technique and the mortality rate in conscious dogs, and to increase the original control series. In all cases the drugs were given before the ligation. Electrocardiograms were taken before and after the administration of the drug, before, during, and for 30 minutes after ligation and then intermittently for some time after the occlusion. The animals were observed clinically and with the electrocardiograph for the 24-hour period. An autopsy was performed immediately on all animals that died.

As previously described (Manning *et al.*, 1939) "sudden death" for the purpose of these studies, means death within the first 24 hours. This period for mortality figures on sudden death following coronary occlusion was adopted by us and by others (Le Roy *et al.*, 1941, 1942; and Gilbert, 1942) because most of the animals that fail to survive, succumb shortly after the occlusion (Table I) and up to the present time these studies have been primarily concerned with the immediate mortality following sudden coronary occlusion. Although long-term studies have not been carried out, it has been observed that if the animal survives the 24-hour period it is unlikely that a cardiac death will occur (Manning *et al.*, 1939; and McEachern *et al.*, 1940).

Results

Control Group. Six of the 8 dogs in which the left circumflex branch was occluded died within the first 24 hours. The sequence of events, including the cardiographic changes, was found to be the same as previously described (Manning *et al.*, 1939; and Le Roy *et al.*, 1941, 1942). In 4 animals ventricular tachycardia and terminal ventricular fibrillation occurred within the first 10 to 12 minutes (Fig. 1 on page 93). Two animals were found dead in 12 to 18 hours following the ligation and the remaining 2 survived. This agrees closely with our earlier results and the findings of others when the left circumflex branch is suddenly occluded in the normal conscious dog. Including the former control series of 16 dogs, the mortality for the untreated group was 18 deaths out of 24 dogs within the first 24 hours, or 75 per cent.

Demerol Series. In these experiments 12 dogs were used. Demerol was given intramuscularly in doses of 10 mg./kilo. followed by a second injection of 5 or 10 mg./kilo. intravenously 15 to 25 minutes later. Ligation of the left circumflex was carried out in the manner described 10 to 20 minutes following the second injection of demerol.

The sequence of events following occlusion was similar to that seen in the control group except that the animals appeared somewhat more disturbed. The incidence and nature of

TABLE I
RESULTS
Showing comparison with previous studies and with those of Le Roy *et al.*, 1942

	Experimental group	Number of dogs	Immediate mortality		24-hour mortality (percentage)	
			Time (min.)	Percentage		
	Control	24	10–12	50	75	
	Demerol	12	2–4	58	58	
	Ergotamine tartrate	13	15	15	70	
	DHE-45	23	2–12	13	30	
1	Bilateral cardio-sensory denervation	22	9–15	9	9	
1	Papaverine	20	17	45	50	
1	Quinidine	20	5	45	55	
2	Control	13	—	—	70	Light anæsthesia
2	Xanthine treated	39	—	—	38	Light anæsthesia
2	Theobromine treated	21	—	—	23	Light anæsthesia
2	Theophylline treated	18	—	—	56	Light anæsthesia
2	Atropine treated	8	—	—	34	Light anæsthesia
2	Atropine	4	—	—	50	
2	Theophylline and atropine	6	—	—	53	

1. McEachern *et al.*, 1940, 1941; Smith *et al.*, 1940.
2. Le Roy *et al.*, 1942.

pain after the occlusion was variable, being the same or greater in 3 animals, absent in 1, and somewhat decreased in the remaining 8. Seven animals died in ventricular fibrillation in 2 to 4 minutes following ligation and the remaining 5 survived the 24-hour period.

The number of animals used does not warrant a statistical comparison of mortality with the control group. However, it would appear that demerol did not afford much protection against cardiac irregularities, tachycardia, and fibrillation, following sudden coronary occlusion. In the cardiogram the effects usually seen following experimental coronary occlusion were observed. There was little or no change in heart rate or rhythm following the injection of demerol. On ligation the typical S–T elevation and T wave changes occurred (Fig. 2); extrasystoles were common. The outstanding feature, however, was the rapid onset of the ventricular tachycardia, which occurred in eleven experiments and terminated in fatal ventricular fibrillation within 2 to 4 minutes in 7 of the 12 animals. In the control group ventricular tachycardia and fatal ventricular fibrillation usually occurred about 10 to 11 minutes following ligation. Four of the 5 dogs that survived did so in spite of the rapid onset of ventricular tachycardia (Fig. 2 on page 93) which in the control experiments was invariably followed by fatal ventricular fibrillation.

Ergotamine Tartrate Series. In these experiments 13 dogs were used. In the first 2 animals 0·5 mg./kilo. ergotamine tartrate was given intravenously. In one of these a severe heart block occurred following the injection of ergotamine and the animal died in fatal heart block 36 minutes after ligation. In view of these effects a dose of 0·25 mg./kilo. was given to the remaining 11 dogs. Nine of the 13 animals died within the first 24 hours. Two dogs died shortly after the ligation, one in ventricular fibrillation in 9 minutes and the other in 36 minutes with heart block following the occlusion. The remaining 7 died in periods ranging from 9 to 18 hours, following ligation (Fig. 3 on page 94). Shortly after the intravenous injection of ergotamine tartrate the animals showed marked muscular weakness, most apparent in the limbs. Increased respiration and dyspnœa, which in several was of an asthmatic nature, were prominent features. Salivation was also observed. Vomiting occurred in two and bowel

evacuation in 5 of the 13 animals. The generalized muscular weakness and dyspnœa continued following the occlusion. Throughout the 24-hour observation period these signs continued and were associated with collapsed peripheral veins and pulseless cold extremities. These effects appeared to increase in severity and approached a maximum some 10 hours following the injection and occlusion. In the animals that did not survive, death occurred suddenly about this time, in the same manner as was seen in other experiments in which the animals succumbed shortly after ligation. In 4 dogs a second injection of ergotamine was given 8 to 10 hours following the ligation, but the terminal event was not delayed any longer.

Following the injection of ergotamine tartrate there was a decrease in heart rate in 12 out of 13 dogs. In 6 of the animals varying degrees of S-A and A-V heart block occurred (Fig. 4). The P–R interval was increased by the drug and the QRS interval showed little or no change. In general the QRS complex and T wave showed inconstant variations in amplitude, the T waves being increased in 2 instances, decreased in 4, reversed in 1, and unchanged in the others. In 3 experiments the RS–T segment was depressed following injection of the drug.

Following ligation there was some increase in the heart rate. Extrasystoles were not seen as frequently as in the control group. The ventricular tachycardia frequently seen shortly after ligation occurred in only one animal, this progressed to fatal ventricular fibrillation in 11 minutes following ligation. One other animal died in heart block (in 36 minutes) which was present even before the ligation. Seven of the 9 dogs that did not survive the experiment died in the 12 to 18-hour period following ligation; 1 died in block, 2 in fibrillation, and 4 were found dead in the cage. In general, the rhythm became regular within half an hour following the occlusion, but was followed by a progressive deterioration which reached a maximum 12 hours later. Wide variations in individual dogs were seen, but the most common findings were varying degrees of S-A, A-V, and bundle branch block. An increase in the number of extrasystoles was also noted and auricular fibrillation occurred in 2 dogs; nodal or extrasystolic rhythm occurred in a few and A-V dissociation was also observed. In contrast to other groups there was following ligation a progressive depression of the RS–T segment which had returned or was approaching the base line again in about 30 minutes. Deeply inverted T waves were also common (Fig. 4 on page 94).

It was apparent that ergotamine tartrate in doses of 0·25 mg./kilo. was effective in inhibiting the mechanism of fibrillation and so reduced the "immediate" mortality. A delayed cardiac death, however, occurred 12 to 18 hours later in 70 per cent of the animals.

Dihydro-ergotamine Series. In these experiments 23 animals were used. DHE-45 was given intravenously (0·4 mg./kilo.) 4 to 5 minutes prior to the occlusion. In the majority of cases some degree of salivation occurred within 1 to 2 minutes, but was less than that seen in the ergotamine series. Gastro-intestinal upsets occurred in 2 instances (retching in one animal and vomiting in another about 3 to 4 minutes following the drug). Bowel movement did not occur before ligation, but was frequent shortly after ligation. Respiration was slightly increased by the drug in a few animals as compared with the marked increase and even dyspnœa seen in the ergotamine tartrate series. The drug appeared to have little or no effect on the pain of ligation. Although most of the animals appeared slightly unsteady following the occlusion, the general collapse and weakness and toxic appearance that was such a prominent feature of the ergotamine series was not apparent. Clinically, these animals appeared more like the control dogs that survived the immediate effects of the occlusion. Seven of the 23 dogs died within the 24-hour period following ligation (30 per cent mortality). Three of these died within 12 minutes following occlusion in ventricular fibrillation (13 per cent). The remaining 4 died in 17 to 19 hours after ligation. A statistical comparison of these results; i.e. 30 per cent of 23 dogs as compared to 75 per cent of 24 dogs in the control group, using the chi square method and the Yates correction for small numbers, yielded a chi square of 7·4 and a P factor of less than 0·01.

In comparison with the ergotamine tartrate series, it is apparent that DHE-45 was not only similar in its protecting action on the ventricular fibrillating mechanism, but also significantly increased the survival rate.

Following the intravenous injection of DHE-45, electrocardiograms were obtained and compared with those taken immediately before giving the drug (Fig. 5 on page 95). In almost every instance there was a slightly decreased sinus rate. In over 50 per cent of records a slight increase in the P–R interval over the pre-drug record was apparent. In the majority of records there was a small increase in the amplitude of the T waves.

Immediately following ligation there was an elevation of the S–T segment in leads I and II, and this was accompanied by a fast sinus rhythm which persisted during the observation period (Fig. 5). The rhythm was broken by bouts of rapidly forming ventricular extrasystoles, or, in many instances, by only an occasional ectopic beat; in three instances ectopic beats did not occur. Within a half-hour the S–T segment had returned to, or was approaching, the pre-ligation base line.

In the animals dying suddenly following occlusion, there were two instances in which a rapid sinus tachycardia was followed by ventricular tachycardia, ventricular fibrillation, and death within 12 minutes (Fig. 5B). The appearance of ventricular tachycardia did not necessarily mean a fatal termination, for in one instance it was seen to appear in 3 minutes and lasted 25 minutes. Tracings taken 24 hours following the ligation showed for the most part a sinus rhythm. Ventricular extrasystoles were frequent, while T waves were inverted and increased in amplitude.

In two instances a ventricular bigeminal rhythm was noted; in one this appeared shortly after ligation, and the animal died in ventricular fibrillation in 11 minutes. The other was observed in the 24-hour record, and the animal survived the experiment. A 2 : 1 A-V block occurred in 13 minutes after ligation in one animal, and S-A block was observed in the 24-hour record of another animal, both of which survived.

Discussion

In previous reports (Manning *et al.*, 1939; and McEachern *et al.*, 1940, 1941) it was suggested that a reflex mechanism that caused constriction of the non-occluded branches, resulting in a generalized ischæmia of the myocardium, may have been responsible for the onset of ventricular fibrillation and the high mortality that followed the occlusion. It was suggested also that the mechanism might be associated with certain areas of myocardium more readily affected by the ischæmic process providing a source for ectopic beats progressing to fatal ventricular fibrillation.

In view of our earlier studies, and the work of others, the prevention of this fatal rhythm seemed to resolve along two pathways. First, by the use of antispasmodic and coronary dilator drugs, which may limit the area of ischæmia to the infarcted portion, and perhaps reduce the amount of non-functioning myocardium. Secondly, by the use of sympathetic inhibiting agents in an attempt to reproduce the results obtained following cardiac sympathectomy (McEachern *et al.*, 1940).

It has been shown that antispasmodic and coronary dilator drugs have some effect in reducing mortality following experimental coronary occlusion (McEachern *et al.*, 1941; Le Roy *et al.*, 1941, 1942; Gilbert 1942; and Gold *et al.*, 1937). Their use in the treatment of coronary occlusion clinically has also been reported (Nathanson, 1936; Gold, 1939; Le Roy *et al.*, 1941; Elek and Katz, 1942; Gilbert, 1942; Falk, 1942; Swanson, 1945; and Gerger, 1945). Consequently, it was anticipated that demerol might decrease the mortality. In these experiments, however, 7 of the 12 dogs died within 4 minutes of the ligation and the remaining 5 survived the observation period. In these 7 cases fatal ventricular fibrillation, recorded by the electrocardiogram, occurred in a shorter period (2 to 4 minutes) than that usually seen in

the control dogs (8 to 12 minutes). Over half of the dogs were hyperexcitable and in general it appeared that the more excitable the animal the earlier was the onset of the ectopic rhythm.

Since the pre-fibrillation ventricular rhythm (and fibrillation) occurred so rapidly following the occlusion, it would seem that demerol increased the excitability of the myocardium. Demerol has been used by Gerger (1945) in acute myocardial infarction and by others for the relief of pain, particularly during labour (Hori and Gold, 1944 ; and Flatt, 1946). In the clinical reports on the use of demerol there appears to be no evidence of the exciting or stimulating effect seen in these experiments.

In the experiments carried out with ergotamine tartrate and DHE-45 the " immediate " (i.e. within the first 15 minutes) mortality was considerably reduced, to 15 per cent and 13 per cent respectively, as compared with the control series mortality of 50 per cent in a similar time. It was shown that this was due to the inhibition of fatal ventricular tachycardia and fibrillation. In the ergotamine tartrate group, the mortality had increased to that seen in the control series by 19 hours after the occlusion ; this we considered due to the combined effect of drug toxicity and infarction. In the DHE-45 experiments, however, the mortality remained low (30 per cent) approximating the results obtained in the cardio-sensory denervation experiments (10 per cent mortality), although pain did not appear to be influenced. Clinically, the DHE-45 experiments resembled the control experiments, except for the mortality rate which was significantly lower in the DHE series.

In the cardiac sympathetic denervation experiments it was postulated that a possible reflex spasm, with the afferent side of the arc in the sympathetic and the efferent radicles in the vagus, was interrupted. An alternative view was that sympathetic denervation rendered the myocardium less susceptible to the onset of ventricular fibrillation (McEachern *et al.*, 1940). Although the former hypothesis has received support (Le Roy *et al.*, 1941, 1942; and Gilbert, 1942), it is difficult, in view of our recent results with DHE-45, to explain the reduction in mortality entirely on this basis, particularly in view of the more recent work on the nervous and reflex control of coronary blood flow (Katz and Joachim, 1939, 1945; and Gregg and Shipley, 1944 and 1946) which, at the present time, is by no means settled (Gregg, 1946).

DHE-45 acts on effector organs in such a way as to render them indifferent to sympathetic impulses (Rothlin and Brügger, 1945). The drug is, therefore, not effective by interrupting the afferent side of such a reflex arc. If sympathetic efferent fibres carry constrictor impulses to the coronary arteries (Katz and Joachim, 1939), then it is still possible that coronary spasm (reflex or otherwise) may be a factor in the onset of fatal tachycardia and fibrillation following coronary occlusion.

The exciting effects of adrenalin and sympathetic stimulation in producing fatal ectopic heart rhythms experimentally (Wiggers, 1930; Naham and Hoff, 1934; Hoff and Naham, 1935; Melville, 1946; and Philips *et al.*, 1946) and the deleterious effects of sympathetic stimulation and adrenalin in coronary heart disease have been described by various writers (Nathanson, 1936; Eppinger and Levine, 1943; and Raab, 1943, 1944, 1945). From the existing evidence it would appear that these effects are the result of a direct action on the heart rather than secondary to a decrease in coronary flow. A similar myocardial excitability follows sudden coronary occlusion and this can likewise be depressed or inhibited by removal of sympathetic nerves or by inhibition of the sympathetic effector mechanism with DHE-45. It would appear reasonable, therefore, to assume that a direct sympathetic excitor mechanism is an important factor in producing the fatal ectopic rhythm following sudden coronary occlusion. In the cardio-sensory denervation experiments both afferent and efferent fibres have been removed. This may be effective through the abolition of reflex constrictor impulses to the coronary bed, or by the removal of the source of adrenalin, both locally in the heart (Hoffmann *et al.*, 1945) and from the adrenals. In the DHE-45 experiments efferent endings only have been affected; pain was unaffected and it is expected that the amount of circulating

adrenalin is high but is rendered ineffective by the DHE-45. It has been shown (Hoff and Naham, 1934) that removal of the stellate ganglia and adrenal glands prevents the occurrence of benzol- and electrically-induced ventricular fibrillation, but that if adrenalin is given to the animal fibrillation occurs. Unfortunately, adrenalin was not given in the cardiac denervation experiments. It is possible, however, that complete cardio-sensory denervation by the abolition of pain prevented the release of adrenalin from the adrenals (or possibly locally in the heart) which must occur with the sudden painful and distressing attack. In this connection it is interesting to note that in the sympathectomized series the 2 animals that did not survive the occlusion died in ventricular fibrillation, and both experienced some degree of pain, indicating that cardio-sensory denervation had not been complete.

Furthermore, from the survival times during the 24-hour period (Table I) it appears, both in these studies and in the previous reports, that the "immediate" mortality (i.e. within the first 15 minutes) in the control group and in the animals treated with antispasmodic and coronary dilator drugs is of the same order. During the remainder of the 24-hour period little or no further increase in mortality occurred in the treated group, whereas in the control group the mortality had increased to 75 per cent. Antispasmodic and coronary dilator drugs, therefore, appeared to have no effect on this "initial" mortality (due to ventricular fibrillation). On the other hand, DHE-45 markedly decreased the early initial mortality (13 per cent), but later in the 24-hour period (18 hours) a small further increase of 18 per cent in mortality occurred.

Although experimental findings in the dog cannot be applied directly to coronary artery occlusion in man, the similarity in clinical features is most striking. There are a number of reports of ventricular fibrillation graphically recorded as the terminal event following sudden coronary occlusion in man (Hamilton and Robertson, 1933; Leary, 1935; Nathanson, 1936; Smith, 1939; Miller, 1939; Le Roy and Snider, 1941; Thompson, 1941; and Falk, 1942). Since most patients suffering a sudden coronary occlusion are not seen by the physician for some time, little is known about the frequency of cardiac irregularities immediately following the attack. In patients who survive the immediate occlusion, frequent extrasystoles, ventricular tachycardia, and other cardiac irregularities that lead to ventricular fibrillation are not considered to be common; in all probability the earlier the patient is seen, the more frequently such irregularities will be observed. Furthermore, when sudden death occurs in such cases some hours or days following the occlusion, a rapid and fatal ventricular tachycardia and fibrillation is responsible (see above). Consequently, if therapy that will inhibit the development of a rapid ectopic rhythm can be instituted early, there may be a reasonable hope of reducing the immediate mortality of sudden coronary occlusion. Experimental and clinical studies suggest that such treatment may be further enhanced by the early use of coronary antispasmodic and dilator drugs, presumably through the favourable effects on coronary circulation.

Summary and Conclusions

Sudden occlusion of the left circumflex branch of the left coronary artery in conscious dogs, resulted in fatal ventricular fibrillation in 75 per cent of 24 animals within the first 24 hours (50 per cent within first 15 minutes). Previous studies (McEachern *et al.*, 1940) have shown that this mortality can be reduced to 10 per cent, or less, if bilateral cardiac sympathectomy is carried out prior to the ligation.

Demerol was not effective in reducing the initial mortality and ventricular fibrillation occurred rapidly in all fatal cases (58 per cent of 12 animals). The 24-hour mortality, however, did not increase further during the 24-hour period. Animals that recovered did so in spite of a rapid ventricular tachycardia although this was invariably followed by fatal ventricular fibrillation when it occurred in the control series.

Ergotamine tartrate prevented the occurrence of post-ligation ventricular tachycardia and

fibrillation in 12 out of 13 dogs. Toxic manifestations were observed in all cases, both clinically and cardiographically, with the result that although survival time was increased the 24-hour mortality rate was unchanged (70 per cent) from that seen in the control group.

Dihydro-ergotamine prevented the occurrence of post-ligation ventricular tachycardia and fibrillation in 20 of 23 experiments. The toxic manifestations seen in the ergotamine tartrate group did not occur. In this group the "immediate" or initial mortality (i.e. within 15 minutes) was 13 per cent and the 24-hour mortality 30 per cent. It is considered that the drug was effective by inhibiting, through its action on the sympathetic efferents, the ventricular tachycardia and fibrillation that result from sudden coronary occlusion.

A discussion of these results, together with other reports on the effect of sympathetic inhibiting agents and coronary antispasmodic and vasodilator drugs in preventing sudden death following acute coronary occlusion is presented.

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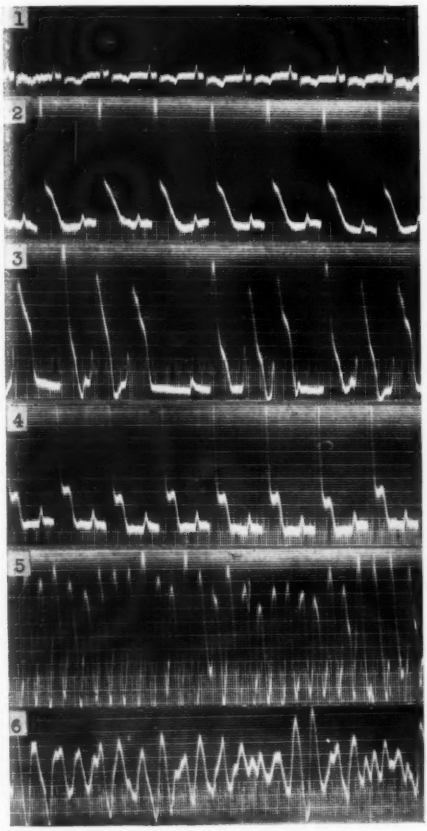


FIG. 1.—Electrocardiograms, lead II, showing typical changes following sudden ligation of the circumflex branch of left coronary artery of the conscious dog (control series). Fatal ventricular fibrillation. (D.3/46.)

(1) Before ligation. (2) Three minutes after ligation. (3) Five minutes after. (4) Eleven minutes after. (5) Twelve minutes after. (6) Thirteen minutes after ligation.

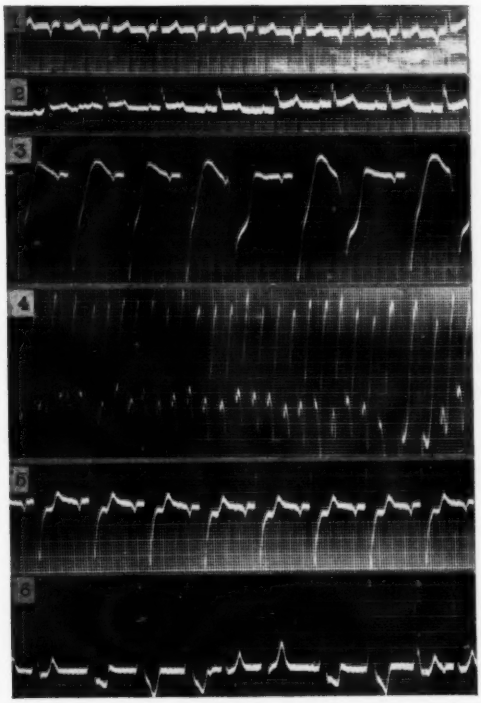


FIG. 2.—Electrocardiograms, lead II, showing typical changes following sudden ligation of the circumflex branch of the left coronary artery of dogs given demerol prior to the occlusion: survival type series of records. Note rapid ventricular tachycardia not followed by ventricular fibrillation, a feature occurring in this group only. (D.19/46.)

(1) Before ligation. (2) Immediately after ligation. (3) Two minutes after. (4) Five minutes after. (5) Twenty minutes after. (6) Twenty-four hours after ligation.

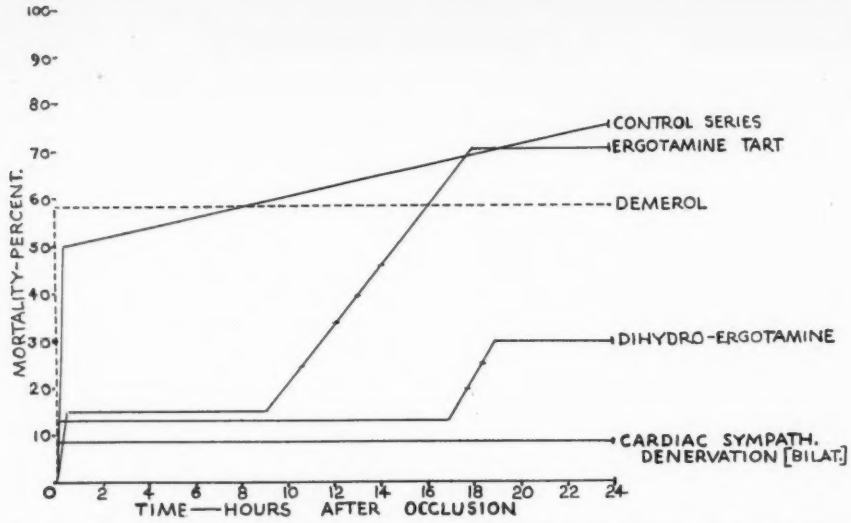
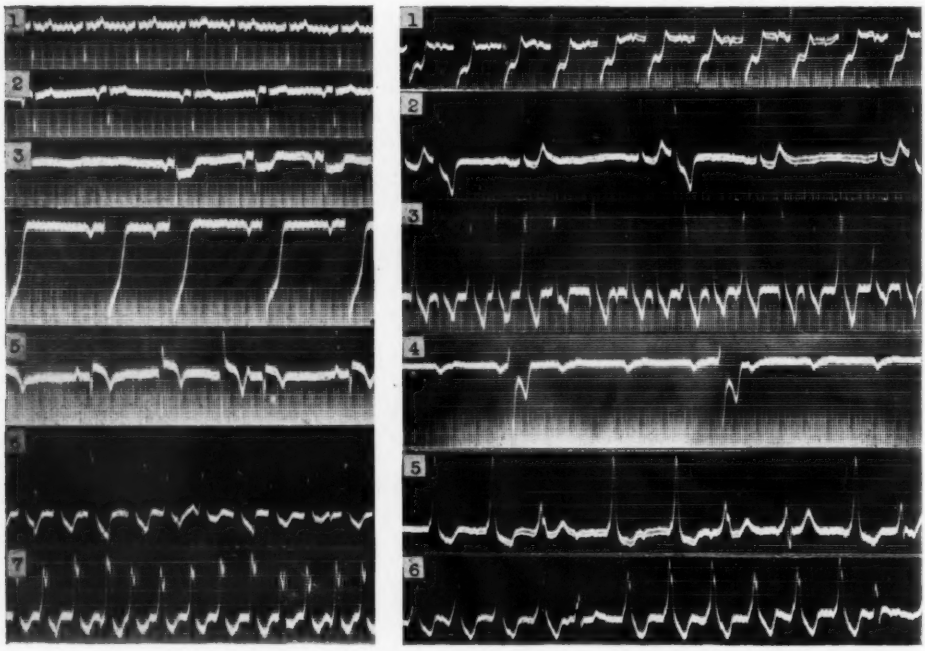


FIG. 3.—Survival times and mortality rates during the 24-hour period following sudden ligation of the circumflex branch of the left coronary artery.



A B

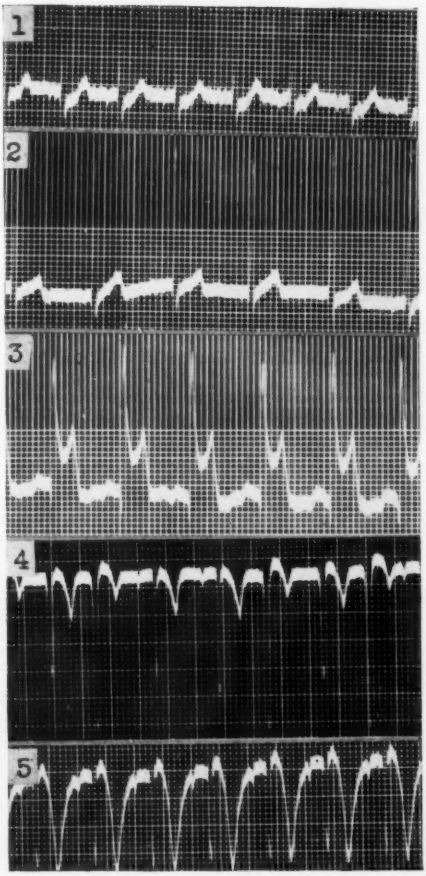
FIG. 4.—Electrocardiograms, lead II, following sudden ligation of the circumflex branch of the left coronary artery of dogs given ergotamine tartrate prior to the occlusion:

(A) Survival type series of records. (D.32/46.)

(1) Before ergotamine. (2) After ergotamine and before ligation. (3) One and a half minutes after ligation. (4) Twelve minutes after. (5) Eight hours after. (6) Seventeen hours after. (7) Twenty-four hours after ligation.

(B) Electrocardiograms from several different dogs showing the various abnormalities that occurred in the ergotamine treated group.

(1) D.28, twenty-five minutes after ligation. (2) D.38, eight-and-a-half hours after ligation. (3) D.33, twelve hours after ligation. (4) D.26, thirty minutes after ligation. (5) D.39, fifteen hours after ligation. (6) D.27, five-and-a-half hours after ligation.



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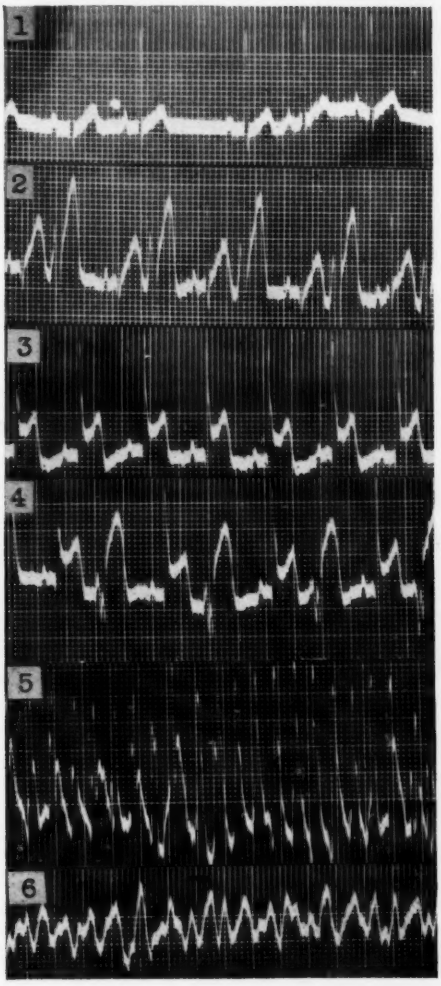

B

FIG. 5.—Electrocardiograms, lead II, following sudden ligation of the circumflex branch of the left coronary artery of dogs given dihydro-ergotamine prior to the occlusion.

(A) Survival type series of records. (D.63/46.)
(1) Before DHE-45. (2) After drug and before ligation. (3) Two-and-a-half minutes after ligation. (4) Twenty-four hours after ligation. (5) Three days after ligation.

(B) Fatal type series of records. (D.47/46.)
(1) Before ligation. (2) Thirty seconds after ligation. (3) One-and-a-half minutes after. (4) Three-and-a-half minutes after. (5) Five minutes after. (6) Six minutes after ligation.

UNUSUAL LONGEVITY IN ANEURYSM OF THE THORACIC AORTA

BY

RALPH KAUNTZE

From St. George's Hospital

Received June 24, 1946

A healthy looking man, aged 36, complaining of recurrent streaking of the sputum with blood and of difficulty in swallowing solids during the previous month was admitted to St. George's Hospital under the care of Dr. F. Golla in 1921. In addition, there had been pains in the back of the head and left side of the neck, which had worried him on occasion since 1919; latterly numbness of the left arm had been noted.

From 1900 to 1919 he had served in the regular Army, contracting enteric and malaria in 1901 while in South Africa. Since 1919 he had been employed as a carman, a not exceptionally strenuous occupation. He had one son alive and well, and his wife had had no miscarriages.

Examination at this time revealed visible pulsation above the manubrium sterni, a tracheal tug, and pulse inequality, the left radial being variable in volume but always weaker than the right. The apex beat was four and a half inches from the mid-line in the fifth left interspace; there was a ringing aortic second sound and an aortic systolic murmur conducted upwards; the systolic blood pressure in the right arm was 132 mm. (that in the left arm was later recorded as 80 compared with 112 in the right arm). There was a systolic murmur over the lower cervical spines and dullness at both lung apices in front, and inequality of the pupils.

The blood Wassermann reaction was positive. The date of primary infection is not known; although his earlier notes give 1900, this is now denied by the patient with some vehemence.

A radiograph with screening was reported as showing a sacculated mass to the left of the aorta in which pulsation was seen, thereby confirming a clinical diagnosis of aortic aneurysm. During this period in hospital his general condition continued poor, the sputum was repeatedly blood-tinged, and at times there was orthopnœa.

From September to December 1921 he received potassium iodide orally and mercury by inunction. In December 0·35 g. of novarsenobenzol was given intravenously, and in the succeeding four weeks a further 2·5 g. His condition at discharge, on January 21, 1922, was noted as " little changed," the sputum being intermittently tinged with blood and the neck pain persisting.

During the subsequent eight months he was confined to bed, after which he slowly started to get about, the sputum being no longer blood-stained. Although he did not attempt any regular work, he remained reasonably well until September 1931 when he again attended St. George's Hospital complaining of giddiness and pains in the chest. There had not been further anti-syphilitic treatment since 1922.

In July 1932 after two short courses of sulphostab and bismuth injections the blood Wassermann reaction was negative. Bismuth injections and mercury by mouth were given at intervals up to 1940, when the blood Wassermann reaction was again negative and the Kahn reaction

positive. Meanwhile, in 1933, he successfully recovered from an operation for acute appendicitis, and in 1934 from an attack of jaundice; at this latter occasion a radiograph showed " a saccular aneurysm with calcification."

In 1941 there were again small hæmoptyses throughout the year. The aneurysm increased in size between 1940 and 1942, when a swelling was noted between the top of the manubrium and the angle of Louis. In April 1944 there was sudden onset of aphasia, possibly embolic in origin, from which recovery has not been complete.

In May 1946 he was admitted to St. George's Hospital under the care of Dr. C. B. Levick, after a sudden increase in the size of the aneurysm; during the previous three weeks there had been weakness of the right arm and forearm, of gradual onset. Occipital and cervical pains were still at times troublesome. The initial symptom, and one that has been present intermittently throughout, was pain in the neck and occiput. The significance of this referred pain in the diagnosis of aneurysm of the aortic arch was emphasized by Graham Steell (1911).

Examination showed slight cyanosis of the lips, a pulsatile swelling four inches transversely

FIG. 1.—X ray of the aneurysm with calcification in the aorta. May 1946.

by three and a half inches longitudinally occupying the whole area of the manubrium, with a weaker and more expansile area in the right periphery; there was no discoloration of the overlying skin.

The pulse was collapsing in type, rate 65–70, the left radial pulse being weaker and lagging behind the right, the pulse inequality being little altered by forced inspiration or expiration. There was dullness from below the right clavicle to the fifth rib extending two inches to the right of the sternum, the apex beat was four inches out in the fifth left interspace, and there were soft aortic systolic and diastolic murmurs: B.P. right arm 175/70, left 155/65.

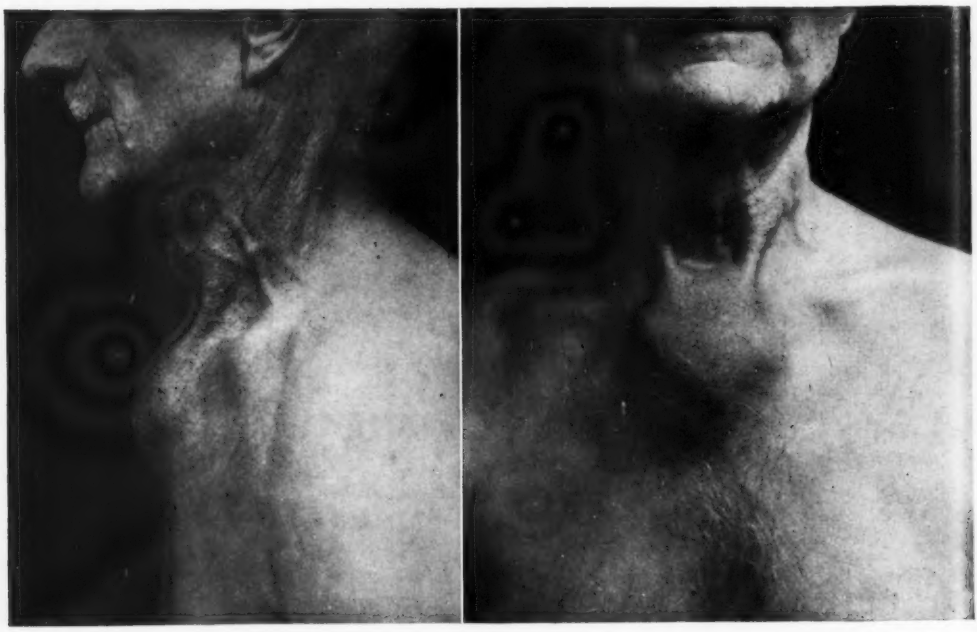

FIG. 2.—Lateral and anterior views of the aneurysm presenting through the manubrium. May 1946.

There were motor aphasia, moderate weakness of all movements of right arm and forearm particularly noticeable in skilled actions, slight wasting of these muscles, hypoalgesia over a small area of the flexor surface of the right forearm, but no positional loss. The abdominal reflexes were absent, the tendon reflexes equal except for ankle jerks which were not elicited, the plantar responses flexor, and the pupils regular, equal, and reacting. There was moderate arteriosclerosis of the retinal vessels and left vitreous opacities. The vocal cords showed normal movements. The weakness of the right arm seemed probably the result of a cortical thrombosis.

X-ray examination showed an aneurysm of the aortic arch, with calcified plaques in the aorta and in parts of the aneurysmal sac; left ventricular hypertrophy; trachea displaced to the right; left diaphragm raised, ? phrenic palsy. By May 15, 1946, a small increase in the size of the visible portion of the aneurysm had occurred, since when there has been little change and equilibrium appears to have been restored. The occipital and neck pains are not now evident, there is no dysphagia, and there is little complaint.

Discussion

The first symptoms referable to the aneurysm occurred in 1919, and in 1921 the lesion was sufficiently advanced to cause dysphagia and hæmoptysis, so that the probable duration in this aneurysm is not less than 27 years. Colt (1926) from a consideration of 482 cases of saccular aneurysm of the thoracic aorta in men found the average duration of life from the onset of symptoms 19 months; among 72 women the duration was 22 months. The expectation of life in aneurysm of the ascending or transverse aorta amongst men with onset at 60 years was rather less than twice that with onset at 35 years: whereas expectation with aneurysm of the descending aorta was the reverse of this.

De Havilland Hall (1913) in 27 private cases gives the duration after diagnosis as 32 months, and suggests that three years represents the average expectation from first symptom; he also mentions an instance of survival for 15 years in a builder's foreman.

Herz (1919) noted a patient, aged 57, with aneurysm of the ascending aorta of 16 years' duration, still alive at the time of the report. Stewart and Garland (1932) record a patient with saccular aneurysm of the aortic arch, first diagnosed at the age of 33, who lived for a further 29 years during which he enjoyed good health, working as a janitor; eventually death resulted from a hypernephroma: he had received iodides for two months and then no further treatment.

Summary

A case of aneurysm of the thoracic aorta of prolonged duration is recorded.

In 1921 the aneurysm was " weeping," but by the end of 1922 the patient was fairly well. Hæmoptysis, after being present in 1921, recurred temporarily in 1934 and again in 1941.

In 1921 treatment consisted of mercury inunctions, potassium iodide, and later five injections of novarsenobenzol, following which there was no further anti-syphilitic treatment until September 1931.

In 1946 his condition is still reasonably good.

I wish to thank Dr. C. B. Levick for permission to publish this case.

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COARCTATION OF THE AORTA: II. CLINICAL FEATURES

BY

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From the Department of Cardiology, University of Manchester

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This paper is concerned with the clinical features of coarctation of the aorta, and is based on a group of 26 cases observed by the author and described in the St. Cyres' Lecture, delivered on June 6, 1945. A paper on the collateral circulation in coarctation of the aorta has been published (Bramwell and Jones, 1941), and a further paper on the radiological diagnosis of the condition will follow: all three are based on the same series of cases.

Coarctation of the aorta has long been familar to anatomists, but until comparatively recently it generally eluded the clinician. In 1928 Maude Abbott was able to collect from the literature 200 cases over three years of age that had come to autopsy; but, of these, only 21 had been diagnosed during life as coarctation and 7 others as obstruction of the aorta. The same year Roesler published his classical paper on the radiological diagnosis of coarctation, and the following year Railsback and Dock published similar observations. Fray added a further paper in 1930.

These radiological observations provided the Mulberry Harbour that enabled clinicians to invade a territory hitherto dominated by morbid anatomists. Many cases have since been reported and I myself have seen 26* in the last fifteen years, 11 in private practice, 8 at my outpatient clinic at the Manchester Royal Infirmary, and 7 in recruits referred to me by medical boards of the Ministry of Labour and National Service during the war.

Autopsy statistics suggest that the incidence of this condition is about one per thousand. Fawcett (1905) found 18 cases in 22,316 autopsies at Guy's Hospital, an incidence of 0·08 per cent, and Evans (1933) 26 cases in 19,217 autopsies at the London Hospital, an incidence of 0·14 per cent; but I am inclined to think that the condition may be more common than these figures suggest, for I have reason to believe that coarctation sometimes escapes detection even at autopsy.

Classification

Most authors have followed Bonnet's (1903) classification and have described two types, the "infantile" and the "adult." In the former, which may be regarded as a persistence or exaggeration of the anatomical relations that exist before birth, there is a diffuse narrowing of the aortic isthmus. In the latter the narrowing, which is in the immediate vicinity of the insertion of the ductus arteriosus, may be so abrupt as to suggest that the aorta had been constricted by a ligature. The adult type was attributed by Craigie (1841) and some subsequent workers to an extension of the normal process that leads to occlusion of the ductus arteriosus after birth. This hypothesis is attractive, but there is considerable evidence in support of the view that the adult form also is due to an error in development at the junction of the primitive fourth and sixth branchial arches, an error that Maude Abbott suggests does not produce its effect till after birth when kinking of the descending limb of the aortic arch results from traction by the obliterated ductus.

* Five more cases seen since May 1945 will be reported later.

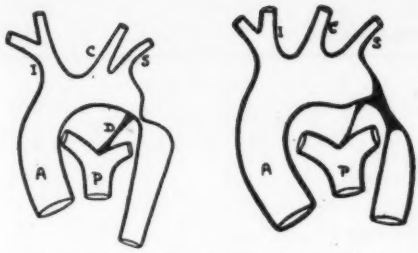

FIG. 1.—Coarctation: Evans's Types 2 and 3.

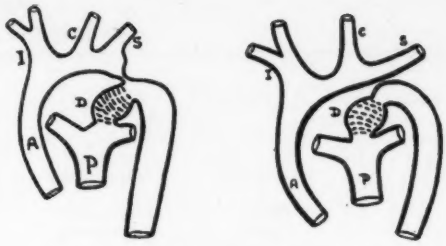

FIG. 2.—Coarctation: Evans's Types 1 and 4.

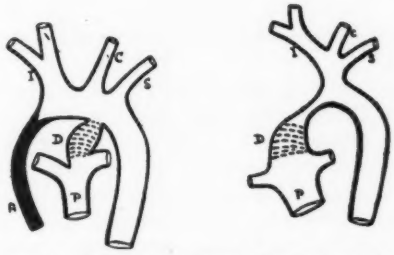

FIG. 3.—Coarctation: Evans's Types 5 and 6.

This classification, though useful, is not entirely satisfactory, and William Evans (1933) suggested an alternative classification based on purely topographical considerations. He described six anatomical varieties of coarctation of the aorta. I would suggest that Evans's classification might, without detriment, be simplified by dividing his six types into three groups. In Group I (Fig. 1), I would place Evans's Types 2 and 3 in both of which the ductus is closed and the proximal portion of the aorta is hyperplastic. Type 3 differs from Type 2 in that the coarctation is complete with atresia of the distal portion of the aortic arch, whereas in Type 2 there is merely a stenosis: this is a difference of degree rather than of kind. Similarly Group II (Fig. 2) would include Evans's Types 1 and 4, in both of which the ductus is patent and the proximal portion of the aorta is hypoplastic. These two types are essentially similar but differ from one another in that in Type 4 the interruption between the arch and descending aorta is complete, whereas in Type 1 there is a narrow communicating channel between them; again a difference of degree. Hypoplasia is rare compared with hyperplasia of the aorta and was present in only 10 per cent of Maude Abbott's cases. Lastly I would place Evans's Types 5 and 6 together in Group III (Fig. 3), since in both the only communicating channel between heart and aorta is the patent ductus. Admittedly there is an important developmental difference between these two types : in Type 5 the proximal portion of the arch is merely atresic or occluded, whereas in Type 6 it is absent.

The expectation of life (Table I) in these three groups is very different. In the first, in which the ductus is closed and the proximal aorta hyperplastic, 7 of Evans's 11 cases reached maturity; of 11 cases in the second group, in which the ductus is patent and the proximal aorta hypoplastic, 1 died in childhood and only 1 reached adult life; while in the third group none of the 6 cases survived infancy. The relatively favourable prognosis in Group I as compared with Groups II and III is probably, in part at any rate, attributable to the fact that the " infantile " type of coarctation is often associated with other grave errors of development, whereas in the so-called " adult " type of coarctation, in which there is an extreme degree of

TABLE I

PROGNOSIS OF EVANS'S SERIES

Group	Type (Evans)	Ductus	Proximal aorta	Coarctation	Age at death			Total
					Infant	Child	Adult	
I	2	Occluded	Hyperplastic	Partial	1	3	7	11
	3	Occluded	Hyperplastic	Complete				
II	1	Patent	Hypoplastic	Partial	9	1	1	11
	4	Patent	Hypoplastic	Complete				
III	5	Patent	Occluded		6	0	0	6
	6	Patent	Absent					
					16	4	8	28

stenosis, this is not the case. Maude Abbott found that of 82 cases in which death occurred within the first year, in 50 (61 per cent) the coarctation was associated with some other major congenital anomaly such as bilocular or trilocular heart, transposition of the arterial trunks, or pulmonary atresia, whereas in 155 cases in which life was prolonged beyond one year an associated major anomaly was present in only 13 (8 per cent) and, in these 13, coarctation was either so slight as to be of no importance or of the infantile type. In the older group, however, other minor congenital defects such as biscupid aortic valve, subaortic stenosis, or abnormal origin of the vessels arising from the arch of the aorta were common and occurred in 57 of the 155 cases.

Clinically, we may divide cases of coarctation into two groups in accordance with whether the ductus is closed or patent. In patients who survive infancy the former is much the more common. In Abbott's series of 200 cases the ductus was patent in only 18 and in my 26 in 3 or possibly 4 cases. The state of the ductus is important ; since a patent ductus provides for the passage of blood from heart to aorta beyond the coarctation and thereby eliminates the necessity for a collateral circulation. Consequently, in such cases, there may be no pulsating vessels on the back or front of the chest and no notching of the ribs. This renders diagnosis more difficult. When the ductus is patent the upper part of the body is supplied by the branches of the aortic arch arising above the coarctation, while the trunk and lower limbs are supplied chiefly by blood entering the descending aorta through the ductus.

CLINICAL MATERIAL

Age. In Table II, I have arranged my cases in accordance with the age at which they first came under observation and have indicated their condition in May 1945: 13 were then alive, 10 had died, and 3 had been lost sight of. These figures are summarized in Table III.

Three of my patients were children, 3 were over 40 years of age, and the remaining 20 were between the ages of 18 and 37 at the time they were first seen. The small number of children in my series is due to the fact that both in hospital and in private practice the great majority of my patients are adults.

Sex. In Abbott's series of 200 cases, one-quarter were females and three-quarters males. If we exclude the 9 " Service cases," drawn from a special section of the population, almost entirely male, the ratio of the sexes in the remainder of my series is 6:11. Why the condition should be so much more common in the male sex it is difficult to say unless it be that, in reality, the sex incidence is equal; but, since women lead a more sheltered life, they are less exposed to the physical strains so often responsible for the development of heart failure in males.

TABLE II

BRAMWELL'S SERIES

Case No.	Sex	Age first seen	After history 1945	
			Age living	Age at death
1	M	9	—	11
2	M	11	—	23
18	M	11	—	12
16	M	18	21	—
20*	M	18	20*	—
22	M	18	19	—
25	M	19	19	—
15	M	20	—	23
14	M	21	25	—
11	M	23	lost sight of	—
24	F	23	—	23
13*	M	24	29*	—
8	F	25	—	27
21	M	26	lost sight of	—
12	M	27	lost sight of	—
23	M	27	28	—
17	M	30	38	—
7	M	31	45	—
4	M	31	39	—
9	F	31	—	36
10	F	32	39	—
19	M	32	35	—
26	F	37	37	—
5	M	46	—	52
3	F	51	—	52
6	M	58	—	62

* See p. 125.

TABLE III

AGE AND PROGNOSIS OF BRAMWELL'S SERIES

Ages in 1945 or at death	Living	Dead	Untraced	Total
10–19	2	2	—	4
20–29	5	4	3	12
30–39	5	1	—	6
40–49	1	—	—	1
50–59	—	2	—	2
60–69	—	1	—	1
Totals	13	10	3	26

This would render it more likely for the condition to remain latent in the female and to pass unnoticed unless it were discovered accidentally in the course of some routine examination. This hypothesis, however, would not account for the high incidence of males in Abbott's series in which the figures are based on autopsy statistics, but for the fact that autopsies are performed less often in the female than in the male. Dr. W. Susman (1946) informs me that in a consecutive series of 2000 autopsies performed at the Manchester Royal Infirmary 63 per cent were males and only 37 per cent females.

Service Cases. Nine of the young adults must be placed in rather a different category from the others since they would not have come under observation but for the war. The lesion in these men was discovered in the course of a routine examination and most of them had been unaware of any disability and had no cause to seek medical advice. Seven were recruits referred to me by recruiting medical boards, one (Case 25) consulted me privately having been rejected for service, and one (Case 21) was a serving soldier referred to my clinic.

TABLE IV

DETAILS OF "SERVICE CASES"

Case	Age	Symptoms	Athletic	Remarks
14	21	Dysp. 2–3 years	+ till 19	
11	23	—	+ at school	
15	20	Septicæmia	+	Aortic incompetence
16	18	Dysp. and pain 2 years	+ at school	
19	32	—	Heavy work	Dyer
20	18	—	++	Swim, rugger, cycle, climb
21	26	Epistaxis	—	Serving soldier
22	18	—	Heavy work	Patent ductus
25	19	—	+	

Six of these men were free from symptoms and had been unaware of any disability prior to the discovery of their cardiac lesion at the medical board. Of the other three, one (Case 14), aged 21, had played football up to the age of 19, but subsequently complained of tiredness and some breathlessness on exertion: another (Case 16), a lad of 18, had complained of dyspnœa and pain in the calves for two years but had played games at school. The third (Case 21) had been known to have heart trouble from childhood, and had always avoided strenuous exertion since it was liable to cause epistaxis.

TABLE V

PERLMAN'S SERIES OF AMERICAN ARMY RECRUITS

Case	Age	Heart disease diagnosed	Athletic
1	28	—	+
2	21	—	+
3	21	—	?
4	19	—	?
5	22	14	++
6	21	early childhood	0
7	20	—	+
8	20	11	0
9	18	—	++
10	23	8	+
11	32	22	+
12	25	early childhood	0
13	18	—	+

It is interesting to compare this group with the series reported by Perlman (1944) from American Army recruits. The ages of the two groups are very similar, 10 of Perlman's cases and 7 of mine being under 25 and none over 33. Seven of Perlman's cases and 6 of mine had no knowledge of heart disease and were free from symptoms; 8 in each series had participated actively in athletics or had been employed in laborious physical work. One of my patients (Case 20) was a good athlete and had gone in for swimming and played Rugby football at the

Manchester Grammar School: he also was a keen cyclist and climbed in Switzerland. One in Perlman's series played semi-professional basket-ball.

Symptoms

The age at which patients first come under observation is a matter of chance, since some seek medical advice for symptoms attributable to their coarctation, others for symptoms due to some intercurrent disease, and in others, unaware of any disability, the lesion is discovered accidentally in the course of a routine examination. The age at which symptoms first appear however, does seem to be of significance in prognosis and I have accordingly classified my cases in three groups.

1. In 5 symptoms dated from childhood. Of these, 2 died in the second decade, 2 in the third, and 1 has been lost sight of.

2. In 11 patients symptoms first appeared between the ages of 16 and 57. Four of these are still alive aged 21, 25, 29, and 37 respectively; 1 has been lost sight of; and the other 6 are dead.

3. Of the remaining 10 patients 1 has been lost sight of and, up to May 1945, the other 9 were either free from symptoms or complained only of symptoms due to some disease unconnected with their coarctation. Their age incidence was from 19 to 45.

Cases in which Symptoms Dated from Childhood

Case 1. A boy; aged 11, was referred to me in December 1934 by Dr. John Ward from the Royal Manchester Children's Hospital to which he had been admitted with a sore throat. Prior to severe epistaxis at the age of 9 he had been free from symptoms. In addition to coarctation, he had subaortic stenosis with great cardiac enlargement (see p. 112). He was readmitted to hospital in May 1936 with acute pericarditis with effusion following a further attack of tonsillitis. From this he made a good recovery, but a few months later developed congestive heart failure from which he died.

Case 8. A woman of 25 consulted me regarding her fitness for pregnancy. Her chief complaint was pain in the back. Two years later she developed subarachnoid hæmorrhage from which she died (see p. 106).

Case 18. This boy appeared to be not only healthy but robust until, at the age of 11, he developed subacute infective endocarditis from which he died. There was evidence, both clinical and radiological, of a patent ductus (see p. 115).

Case 21. A serving soldier was referred to my clinic by Major Olav Kerr, R.A.M.C. Since childhood he had always avoided strenuous exertion since it was liable to produce epistaxis. After three years' service as a draughtsman he decided to take a sapper's course for promotion, but this proved too strenuous for him and provoked dyspnœa. Shortly afterwards he was invalided out of the service following pneumonia and has since been lost sight of.

Case 24 (see p. 113). A woman of 23 had been short of breath as long as she could remember and cyanosed in cold weather. While in hospital she had two peculiar attacks in which she complained of paræsthesia in the lower limbs associated with a feeling of constriction in the lower sternal region. Following her second attack she developed œdema and died of congestive heart failure. In this case the presence of a widely patent ductus (Fig. 6) was confirmed post-mortem and the coarctation was of the infantile type.

Cases in which Symptoms Developed Later in Life

Case 2. A boy of 11 was referred to me in 1930 on account of palpitation following a minor gastro-intestinal disturbance and was found to have coarctation of the aorta. Throughout his time at the Manchester Grammar School he had no illness, and played cricket and swam. He remained free from symptoms till 1942 when he developed subacute infective endocarditis from which he died.

Case 3. A woman aged 51 first noticed tightness in the chest and palpitation at the age of 50. She had worked hard all her life and had never required medical attention previously, but had always preferred a standing job as she got pain in the left chest if she had to sit for long (see p. 107).

Case 5 (see p. 107). A man, aged 46, was referred to me complaining of a pain in the right arm of twelve months' duration. When seen again four years later the pain had ceased to trouble him and he died of carcinoma of the stomach at the age of 52.

Case 6 (see p. 112). In March 1933, I was consulted by a man of 58 who had enjoyed good health and led an active life until twelve months previously, when he began to suffer from dyspnœa on exertion with a sensation of constriction in the chest. Six months later he developed auricular fibrillation and shortly afterwards had a severe coronary occlusion. In June 1935 he was still fibrillating but free from symptoms and able to carry on his business. He died of lobar pneumonia at the age of 62. This man's freedom from symptoms was remarkable as, in addition to his coarctation, he had aortic incompetence and his heart was greatly enlarged. Two years before death he underwent a major operation from which he made an excellent recovery.

Case 9 (see p. 122). A woman, aged 31, first noticed shortness of breath in the fourth month of pregnancy. She was successfully delivered by Cæsarean section. Two years later she again became pregnant and developed auricular fibrillation. She died from congestive heart failure at the age of 36.

Case 12. A varnish maker, aged 27, was referred to me by my colleague, Dr. A. Hillyard Holmes, whom he consulted on account of tiredness and attacks of vomiting a month previously. Only since this attack had he been short of breath and suffered from palpitation. This case has been lost sight of (see p. 107).

Case 13. A storekeeper, aged 24, was referred to me on account of high blood pressure. He had suffered from epistaxis since the age of 13, but had played football regularly until a year before I saw him, in spite of the fact that since 17 he had complained of pain in the back which troubled him intermittently. As this man's only symptom prior to the age of 17 was epistaxis, and since he had participated actively in athletics up to the age of 23, I have not included him in the group of cases in which symptoms dated from childhood (see p. 107 and 125).

Case 14. A leather worker, aged 21, who had been short of breath and easily tired for 2 or 3 years, prior to which he had been perfectly well and played football, was referred to me by a recruiting medical board in 1940. In May 1945 he was feeling fit and still anxious to join the Navy. In this case it is very doubtful whether the temporary asthenia in 1938–40 was attributable to his coarctation.

Case 15. A shop assistant, aged 22, was referred to me by a medical board in April 1941. He had always enjoyed excellent health and gone in for football, cricket, rowing, and cycling. He was admitted to Crumpsall Hospital in March 1944 and I am indebted to the Superintendent, Dr. Ramsay, and to Dr. R. W. Luxton, for particulars of his illness at that time. Blood culture on two occasions yielded *Staphylococcus aureus* and he was considered to be suffering from septicæmia. He died five days later, but unfortunately permission for a necropsy was not obtained. This young man never had any symptoms until ten days before his death. His coarctation was unsuspected at the time of his acute fatal illness, which may have been acute infective endocarditis.

Case 16. An accountant's clerk, aged 18, who had played tennis and cricket at school, began to complain of breathlessness and pain in the calves on exertion at the age of 17. He was referred to me by a medical board in January 1942: in May 1945 he informed me that, though he had occasionally complained of tiredness he had not been off work.

Case 26. A woman, aged 37, complained of slight dyspnœa on exertion, but otherwise, apart from an illness 17 years previously, had been free from symptoms excepting during her two pregnancies (see p. 121).

Discussion of Symptoms

To summarize these findings, the symptoms of which my patients chiefly complained were as follows:

Three (Cases 2, 15, and 18) were free from symptoms until they developed infective endocarditis or septicæmia, three (Cases 1, 13, and 21) complained of repeated epistaxis, and one (Case 8) of migraine dating from childhood; it is interesting to note that she died of subarachnoid hæmorrhage. Breathlessness and palpitation on exertion were common symptoms as was undue tiredness. Eight of my patients complained of pain which affected various parts of the body. This symptom merits more detailed consideration.

Case 8. A parson's wife, aged 25, consulted me in July 1938 regarding her fitness for pregnancy. In childhood she suffered from migraine and at school she was never able to play games because of

dyspnœa and palpitation. From 17 until her marriage at 24 she worked in an office and was never absent owing to illness except for occasional sore throats. When I saw her she was able to do all her housework with the help of a woman on one half-day a week, but complained of pain below the angle of the left scapula aggravated by exertion and occasional dyspnœa and palpitation. Apart from the pain in the back, she remained fairly well until 1940, when she had a subarachnoid hæmorrhage from which she died. The post-mortem findings in this case have been fully reported (Bramwell and Jones, 1941).

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Case 5. A medical practitioner, aged 46, was referred to me in January 1934 by my colleague, Dr. Fergus R. Ferguson, whom he had consulted the previous November for an aching pain of twelve months' duration, felt in the region of the insertion of the right deltoid, the outer side of the forearm, midway between the wrist and elbow, and in the tips of the fingers. It occurred at any time of the day or night, but was aggravated by using the arm driving his car which had a right-hand gear change. For twelve years he had been subject to cramp in the right arm and for five years his handwriting had been somewhat shaky. Having had chorea at the age of 14, he had been stopped playing games at school on account of his heart, but later played tennis. Following influenza in 1923 he had suffered from asthma until 1930. I obtained no history of other illness. His biceps and supinator jerks were diminished on the right side, but the triceps jerk was normal. On a neurological basis, Dr. Ferguson considered that the signs and symptoms could only be accounted for by the somewhat unsatisfactory diagnosis of " brachial neuritis " and he was inclined to think that pressure from the dilated arteries on the nerves of the brachial plexus was a more plausible explanation. This, however, seems doubtful, for when seen again in May 1938 he stated that the pain in the arm had ceased to trouble him. He eventually died of carcinoma of the stomach at the age of 52.

Case 12. A man of 27 complained of attacks of præcordial pain passing through to the back, on account of which he was suspected of aneurysm.

Case 13. A storekeeper, aged 24, began to complain of pain in the back at the age of 17. Nevertheless he continued to play football regularly until twelve months before I saw him. He then gave it up, not on account of the pain, but because it made him unduly tired. The pain was most severe when he first got up in the morning and passed off in about half an hour. At the age of 22 he had a course of treatment from an osteopath over a period of 18 months and was then told he had a high blood pressure. Hence he consulted me. When I last heard of him five years later he stated that he was feeling quite well. The introspective nature of this patient made me inclined to discount his symptoms to some extent.

In two of the four cases reported by King (1926) pain was a prominent symptom. One of his patients, a man of 35, complained of pain on exertion in the left side of the chest, and a year later in the right chest. In King's other patient, a man of 58, the pain was in the left supra-clavicular fossa and left shoulder. One of Evans's (1933) patients complained of pain along the left border of the scapula. In both these cases the pain corresponded in position to areas of arterial pulsation.

Enlarged collateral channels might produce pain in several ways. Evans (1933) suggested

Case 5 (see p. 107). A man, aged 46, was referred to me complaining of a pain in the right arm of twelve months' duration. When seen again four years later the pain had ceased to trouble him and he died of carcinoma of the stomach at the age of 52.

Case 6 (see p. 112). In March 1933, I was consulted by a man of 58 who had enjoyed good health and led an active life until twelve months previously, when he began to suffer from dyspnœa on exertion with a sensation of constriction in the chest. Six months later he developed auricular fibrillation and shortly afterwards had a severe coronary occlusion. In June 1935 he was still fibrillating but free from symptoms and able to carry on his business. He died of lobar pneumonia at the age of 62. This man's freedom from symptoms was remarkable as, in addition to his coarctation, he had aortic incompetence and his heart was greatly enlarged. Two years before death he underwent a major operation from which he made an excellent recovery.

Case 9 (see p. 122). A woman, aged 31, first noticed shortness of breath in the fourth month of pregnancy. She was successfully delivered by Cæsarean section. Two years later she again became pregnant and developed auricular fibrillation. She died from congestive heart failure at the age of 36.

Case 12. A varnish maker, aged 27, was referred to me by my colleague, Dr. A. Hillyard Holmes, whom he consulted on account of tiredness and attacks of vomiting a month previously. Only since this attack had he been short of breath and suffered from palpitation. This case has been lost sight of (see p. 107).

Case 13. A storekeeper, aged 24, was referred to me on account of high blood pressure. He had suffered from epistaxis since the age of 13, but had played football regularly until a year before I saw him, in spite of the fact that since 17 he had complained of pain in the back which troubled him intermittently. As this man's only symptom prior to the age of 17 was epistaxis, and since he had participated actively in athletics up to the age of 23, I have not included him in the group of cases in which symptoms dated from childhood (see p. 107 and 125).

Case 14. A leather worker, aged 21, who had been short of breath and easily tired for 2 or 3 years, prior to which he had been perfectly well and played football, was referred to me by a recruiting medical board in 1940. In May 1945 he was feeling fit and still anxious to join the Navy. In this case it is very doubtful whether the temporary asthenia in 1938–40 was attributable to his coarctation.

Case 15. A shop assistant, aged 22, was referred to me by a medical board in April 1941. He had always enjoyed excellent health and gone in for football, cricket, rowing, and cycling. He was admitted to Crumpsall Hospital in March 1944 and I am indebted to the Superintendent, Dr. Ramsay, and to Dr. R. W. Luxton, for particulars of his illness at that time. Blood culture on two occasions yielded *Staphylococcus aureus* and he was considered to be suffering from septicæmia. He died five days later, but unfortunately permission for a necropsy was not obtained. This young man never had any symptoms until ten days before his death. His coarctation was unsuspected at the time of his acute fatal illness, which may have been acute infective endocarditis.

Case 16. An accountant's clerk, aged 18, who had played tennis and cricket at school, began to complain of breathlessness and pain in the calves on exertion at the age of 17. He was referred to me by a medical board in January 1942: in May 1945 he informed me that, though he had occasionally complained of tiredness he had not been off work.

Case 26. A woman, aged 37, complained of slight dyspnœa on exertion, but otherwise, apart from an illness 17 years previously, had been free from symptoms excepting during her two pregnancies (see p. 121).

Discussion of Symptoms

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that pain in the back in patients with coarctation might be due to erosion of ribs by the enlarged intercostal arteries, like the pain produced by an aneurysm of the aorta which erodes the vertebræ, but the frequency with which well-developed rib notching is present without pain makes this explanation improbable.

Pain in the arm or around the costal margin is more suggestive of root or nerve pressure. This might be due either to direct pressure on nerve trunks or to pressure by the enlarged anastomotic artery where it passes through the intervertebral foramen.

The importance of the spinal anastomosis in coarctation of the aorta has not been generally appreciated. The vertebral artery, arising from the first part of the subclavian, reinforces the spinal arteries in which the blood flows downwards to reach the spinal branches of the aortic intercostals. These pass through the intervertebral foramina. There are also branches from the inferior thyroid artery which pass through the intervertebral foramina in the neck to join the spinal arteries.

A patient reported by Haberer (1903) is of unusual interest in this connection. Three days before admission to hospital she developed transverse myelitis from which she died three months later. At autopsy it was found that the anterior spinal artery had contributed to the collateral circulation and had caused compression of the spinal cord at the level of the second dorsal segment. In spite of atresia of the aorta, this woman had borne seven children.

The association of the pain with exertion can be explained by the increased blood flow through the tortuous and pulsating collateral channels, and the differing sites of pain may be related to differences in the anastomotic pattern.

In view of the low blood pressure in the lower limbs, one would have expected intermittent claudication to be common in patients with coarctation of the aorta, but only two of my patients complained of pain or paræsthesia in the legs—an army recruit who had played games at school, and had complained of pain in the calves on exertion since the age of 17 (Case 16) and a young woman with coarctation and a patent ductus who suffered from peculiar attacks of paræsthesia, associated with a sensation of heaviness but not actual pain in the lower limbs (Case 24).

In both cases reported by Blumgart, Lawrence, and Ernstene (1931) occasional cramp in the legs was complained of. King (1926), Parsons-Smith (1921), and Woltman and Sheldon (1927) each reported a case with intermittent claudication and in Gossage's case (1913) the patient suffered all his life from weakness in the legs.

Cases in which there were no Symptoms

It is surprising how many patients with coarctation of the aorta are not only free from symptoms, but reach a high standard of physical and mental development. Maude Abbott refers to the case of a university professor "who presented no signs of failing circulation unless his remarkable mental development and an unusually lively and restless nature were signs of an arterial hyperæmia of the brain."

Nine of my patients were free from symptoms in May 1945 and of these 5 were over 30 years of age. In addition there were 3 (Cases 6, 3, and 5) who reached the ages of 57, 50, and 45 respectively before symptoms developed. Three young recruits (Cases 20 (see p. 125), 22, and 25) and the following 6 older patients are known to have been symptom-free up to May 1945.

Case 4. A man, now 39 years of age, who has had no symptoms directly attributable to his coarctation, was referred to me in 1937 by my colleague, Professor E. D. Telford, whom he had consulted on account of incipient gangrene of the terminal phalanx of the middle finger of the left hand. This he attributed to an accident two years before in which the nail had been torn off: examination, however, revealed a predisposing local lesion in the left arm, namely congenital phlebarteriectasis. In 1938 he was admitted to the Middlesex Hospital where the affected finger was amputated. When I last saw him in May 1945 he stated that since 1941 he had held a clerical job and had been off work

only one day. The left arm still ached at times and this occasionally kept him awake at night. The aching was relieved by elevating the limb. The symptoms in this case may have been entirely attributable to his phlebarteriectasis.

Case 7. A business man, who is now 45, never had any symptoms apart from occasional extrasystoles. He first consulted me in 1931 as high blood pressure had been discovered in the course of a routine examination. There was nothing of significance in his medical history and he was able to play a hard game of tennis. When I last heard of him, in 1945, he stated that he had not felt better for years. He worked hard during the war, his hours were long, and he could dig for long periods in his garden—a large one which he kept entirely unaided.

Case 10. This woman is living and well at the age of 39 (1945). She was referred to me on account of thyrotoxicosis in 1938. Before this she had been very fit and during the summer of 1937 had played tournament tennis. The thyrotoxicosis was cured by a course of X-ray treatment. Since then she has been free from symptoms and during the war has engaged in Red Cross work in addition to her housework and has undertaken the active charge of a large garden which has entailed a lot of heavy digging (see p. 112).

Case 17. An assistant works manager in a big industrial firm, now aged 38, consulted me in 1937 having been refused a pilot's licence on account of high blood pressure, though he had previously served in the Oxford University air squadron. He was able to play tennis and squash without the least discomfort, and during the war he became a platoon sergeant in the Home Guard, but retired after three years' service on account of insomnia, which he wisely regarded as a warning to avoid violent exertion. Since then he has had no further trouble and has been able to deal with the strenuous conditions of war-time factory management.

Case 19. A dyer, aged 32, who was employed during the war as a foundry labourer, was referred to me by a medical board in 1942. All his life he had done laborious work and had never been conscious of any disability. He wrote me in 1945 saying that he still kept perfectly fit. He was working seven days a week and would have liked to get into the army.

Case 23. A man, aged 27, consulted me on account of a murmur, due to a patent ductus. He also had coarctation of the aorta, but neither lesion had ever caused any disability. (See p. 115.)

To sum up, 9 of the 23 cases which it has been possible to follow up were free from symptoms in May 1945 and 5 of these were then over 35 years of age. In addition 3 other patients in my series did not develop symptoms till after the age of 45.

To look at the problem from another angle, if one excludes the 3 who have been lost sight of, the remaining 23 in my series may be divided into three groups in accordance with their age at the present time. Three lived to over 50 years of age. All three are now dead, but two died of conditions unconnected with their coarctation, namely carcinoma of the stomach and lobar pneumonia. None of them had any symptoms before the age of 45 and one lived to 62. Between 30 and 50 there are 7 cases. Of these one died at 36, after her second confinement; the other 6 are alive and 5 have been free from symptoms up to the present time. Of the 13 cases under 30 years of age, 6 have died and 7 are living, 4 of the latter being free from symptoms.

TABLE VI

PROGNOSIS OF AGE GROUPS (BRAMWELL)

	Dead	Symptoms	No symptoms	Total
Over 50	3	—	—	3
30–50	1	1	5	7
10–30	6	3	4	13
Totals	10	4	9	23

The third decade appears to be the dangerous period, and this is not surprising for it is then that the men are exposed to the greatest physical strain and the women are likely to have their first pregnancy, while subacute infective endocarditis is common at this age.

The number of patients over 30 years of age who are not merely free from symptoms but able to undertake considerable physical activity suggests that when the coarctation is sufficiently well compensated to surmount the hazards of the third decade it may cause little trouble until the degenerative period of life.

Diagnosis

The classical signs of coarctation are (1) high arterial pressure in the upper limbs associated with lower pressure in the lower limbs, (2) pulsating arteries on the back or front of the chest, and (3) rib notching as shown by radiography. One or more of these signs may be absent: in some cases there is no clinical evidence of a collateral circulation and the ribs are not notched, and occasionally the blood pressure is not above normal.

To these signs I would add two others that are unlikely to escape detection in the course of an ordinary routine examination—excessive arterial pulsation at the root of the neck and a systolic murmur, the distribution of which does not conform to that of the common valvular or congenital lesions; this murmur may be very clearly heard, in fact it is sometimes loudest, in the interscapular region. There is also a radiographic abnormality that may be of diagnostic importance when rib notching is absent—a double aortic knuckle.

The Arterial Pressure. As Lewis (1934) pointed out, unless the possibility of coarctation be kept in mind in all cases of unexplained hypertension, the condition is apt to escape recognition, and palpation of the femoral pulse should be included in the routine examination of all such cases. I would add that in order to avoid missing coarctation the blood pressure in the lower limbs should be taken in all cases of patent ductus and in those cases of aortic incompetence in which the ætiology is obscure.

Occasionally the blood pressure in the upper limbs is not raised. In Case 10 in my series it was 140/90 and in Case 2 it fell from 165/90 to 130/60 when subacute infective endocarditis supervened. In one of the children in my series (Case 1) in whom the coarctation was associated with subaortic stenosis the pressure was only 95/75. Hallock and Hebbel (1939) reported a case without hypertension: in one of King's (1937) cases the blood pressure was only 123/87 and in Case 12 of Blackford's (1928) series, a man of 24 who had served in the American Navy, the pressure was 128/88.

The Collateral Circulation. The collateral circulation in coarctation of the aorta was first described by Paris in 1791. Unless the back and front of the chest be inspected carefully in a good light, pulsating arteries can easily be overlooked. In one of my patients (Case 9) in whom the collateral circulation had been quite obvious when the heart rhythm was normal, pulsation could only be detected by very careful palpation when auricular fibrillation supervened.

A late systolic murmur is generally audible over the dilated arteries that form the collateral circulation and may be heard on the back of the chest even when no pulsation is palpable. When the internal mammary and deep epigastric anastomosis is well developed, the peculiar distribution of the murmur, which is equally well heard on both sides of the chest in an area parallel to the border of the sternum, can hardly fail to attract attention.

The superficial anastomosis is no sure indication of the extent of the anastomosis as a whole. In Case 8 in our series, which came to autopsy, one of the most important anastomoses proved to be between the superior intercostal, arising proximal to, and the aortic intercostals, arising distal to the coarctation. This anastomosis is deeply situated and is inaccessible to palpation. It is not surprising that these vessels should be greatly dilated since they provide the shortest route to circumvent the coarctation, and when this route is freely patent the femoral pulse may be of good volume even though there be complete atresia of the aorta. When on the other hand the blood has to follow a more circuitous route to reach the descending aorta, the volume of the femoral pulse is correspondingly reduced; for, as Bonnet pointed out, the

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The Publishers regret that, owing to the difficulty of obtaining sufficient supplies of art paper, it will be necessary for the present to print the text of the *British Heart Journal* on a lighter paper and to reserve the art paper for half-tone illustrations in which fine detail has to be shown. This is an emergency measure, and it is hoped soon to return to normal conditions.

sensation conveyed to the finger by palpation of the pulse depends, not on the blood flow, but on the steepness of the pressure gradient along the front of the pulse wave: the volume of the femoral pulse bears no relation to the degree of stenosis of the aorta.

In normal subjects the femoral and radial pulses are synchronous on palpation, but in many cases of coarctation the femoral pulse appears to be delayed. This is due to the fact that it is not the arrival of the pulse wave in the artery, but the crest of the wave that is appreciated on palpation and, in coarctation, the pulse in the lower limb is of the slowly rising type.

Other problems relating to the collateral circulation are more fully discussed in our previous paper (Bramwell and Jones, 1941).

Radiological Diagnosis

The discovery that rib notching could be demonstrated radiographically was a great stimulus to the diagnosis of coarctation of the aorta. Prior to the publication of Roesler's paper very few cases had been recognized during life. Rib notching does not occur in every case, and is absent when the coarctation is associated with a freely patent ductus arteriosus. Well-developed rib notching was present in 17 of the cases in my series: in 5 (Cases 11, 17, 20, 21, 22) it was not sufficiently definite to be of diagnostic value and in 4 it was absent; two of these (Cases 1 and 18) were children and in 3 of the 4 (Cases 18, 23, and 24) the ductus was patent.

Laubry's (1937) suggestion that rib notching is not pathognomonic of coarctation led us to make further observations on the point. These have convinced us that the trivial degree of notching occasionally met with in other conditions is easily distinguished from the notching of coarctation.

The absence of the aortic knuckle has been stressed by most writers as an important radiological sign, the vascular pedicle being funnel shaped; but, although this is a striking feature in some cases, in others, prominences that may easily be mistaken for the aortic knuckle are produced by other structures.

Direct demonstration of discontinuity of the aorta with the patient in the left oblique position is theoretically the most convincing proof of coarctation, but in our experience this is rarely possible even by the use of tomography. Fray (1930) states that a defect in the aorta can be demonstrated in all cases in which it is possible to obtain a satisfactory left oblique film, but his statement appears to be based on only two cases. Taylor (1934), on the other hand, was unable to demonstrate discontinuity in any of her five cases, Roesler (1943) agrees that it is sometimes impossible, especially in young subjects, and Brown (1939) states that even in the adult it can rarely be demonstrated.

When rib notching is absent, the most important radiological sign of coarctation is the presence of a double prominence in the region of the aortic knuckle (Fig. 4 and 7), the upper component being formed by the dilated left subclavian artery where it arises from the blind end of the aorta proximal to the coarctation, and the lower component by the blind end of the descending aorta. This and other aspects of the radiological diagnosis will be more fully discussed in a subsequent paper.

In five of the cases in the present series the diagnosis was made by the radiologist (Table VII). In one (Case 6) the clinical signs were attributed to associated aortic regurgitation, in another (Case 10) in which the blood pressure was only 140/90 to Graves's disease, while in a third (Case 1) they were overshadowed by those of subaortic stenosis. It is in cases such as these, in which some additional lesion is present, that coarctation is especially liable to be overlooked. The other two cases were referred to me by my colleagues after the condition has been diagnosed radiologically—Case 5, with pain in the arm which it was thought might

TABLE VII

CASES DIAGNOSED BY RADIOLOGY

Case	Sex	Age	Clinical diagnosis	Radiology
6	M	58	Aortic incomp.	Rib notching
10	F	31	Thyrotoxicosis	Rib notching
1	M	9	Subaortic stenosis	Double knuckle
5	M	46	? Cervical rib	Rib notching
12	M	27	? Aneurysm	Rib notching

be due to a cervical rib, and Case 12, where the physical signs suggested the possibility of aneurysm of the aorta.

In Case 6, aged 58, the heart was greatly enlarged, he had an aortic diastolic murmur, and the blood pressure was 200/80. No subcutaneous arterial anastomosis was detected, but X-ray examination showed notching of the ribs and absence of any aortic knuckle or aortic impression on the œsophagus. Clinically this appeared to be a straightforward case of aortic incompetence with auricular fibrillation, but there was one feature that should have led us to suspect coarctation—the high systolic pressure. In aortic incompetence due to rheumatic infection, syphilis, or arteriosclerosis, the systolic pressure rarely exceeds 170.

In Case 10, referred on account of thyrotoxicosis, arterial pulsation in the neck was excessive but this did not arouse my suspicion, as I attributed it to the overacting heart, and the blood pressure was only 140/90. I referred her to Dr. E. W. Twining for X-ray treatment and it was he who made the diagnosis. Thinking that the carotid pulsation was more than could be accounted for by the thyrotoxicosis, he took a film of the chest which showed typical rib notching. This was the only adult patient in my series in whom the blood pressure was not at any time found to be above normal.

The association of thyrotoxicosis with coarctation is interesting. Cookson (1936) who reported a case of coarctation of the aorta with toxic goitre, treated by complete thyroidectomy, suggested that the association is too frequent to be fortuitous. In support of this hypothesis, he refers to papers by Loriga (1887), Blackford (1928), Ulrich (1931), Amberg (1932), Eppinger and Midelfart (1933) and Brown (1934). Of the 9 cases reported by these authors, 7 were females. Cookson suggests that the mechanism by which thyroid disturbance arises in association with coarctation is the increased blood supply to the gland, as a result of the collateral circulation through the superior and inferior thyroid arteries which arise from the external carotid and subclavian respectively, above the coarctation.

In the fifth case, diagnosed by radiology (Case 1), the apical cardiac impulse was in the anterior axillary line and a second impulse and systolic thrill were palpable to the right of the manubrium. A to-and-fro murmur was audible over the manubrium and a systolic murmur on the back of the chest. The blood pressure was 95/75 and the femoral pulse was of good volume. Dr. Evan Bedford kindly gave me his opinion on the interpretation of the unusual X-ray appearances in this case (Fig. 4). He considered that the double aortic knuckle signified coarctation of the aorta, the upper knob corresponding to the blind end of the aortic arch and the lower one to the blind end of the descending aorta. My colleague, the late Dr. E. W. Twining made an exhaustive tomographic investigation of this case and satisfied himself that this explanation was correct. I have since been struck by the extraordinary similarity of this radiogram to that in Hamilton and Abbott's (1928) case.

COARCTATION ASSOCIATED WITH PATENT DUCTUS

The diagnosis of coarctation when associated with a patent ductus may be very difficult.

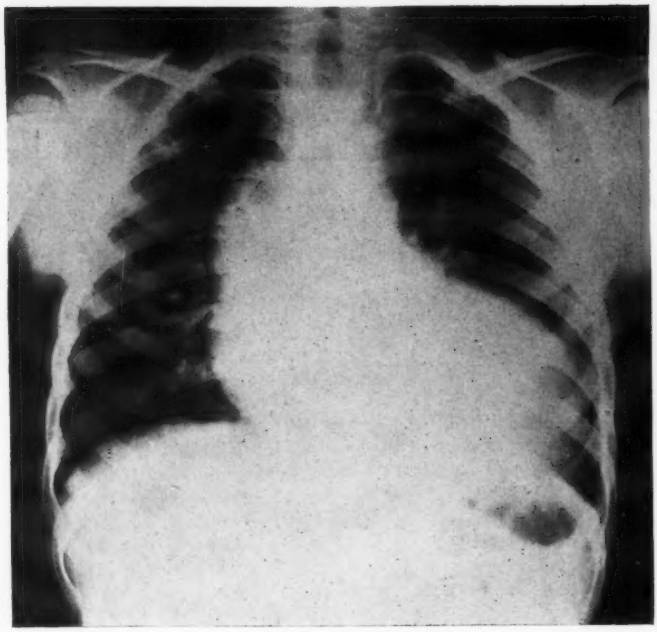

FIG. 4.—Radiogram Case 1, showing double aortic knuckle (see text).

The first case was diagnosed post-mortem, the second clinically, and in the third, a child, the diagnosis was suspected.

Case 24. An unmarried woman, aged 23, was admitted to hospital from my outpatient clinic on November 26, 1941, complaining of dyspnœa and œdema of the feet. She had been short of breath as long as she could remember and cyanosed in cold weather since birth. These symptoms had been worse during the past year. In July 1941 she had been admitted to Withington Hospital with retention of urine and acute respiratory distress and I am indebted to the Medical Superintendent, Dr. Greenwood, for information regarding her condition at that time. She then had œdema of the feet and complained that she had " no use in her legs." Her symptoms were relieved by catheterization.

The heart shadow (Fig. 5) was globular with generalized cardiac enlargement, but no rib notching. Auscultation revealed triple rhythm at the apex and a harsh murmur extending from systole into diastole, but chiefly diastolic, maximal in the third left intercostal space close to the sternum. Moist sounds were present at the bases of the lungs, and the liver was slightly enlarged. Her systolic pressure was 170, but the diastolic end-point was indefinite.

On November 28 she complained of tingling starting in the left foot, then affecting the right foot, spreading up to the thighs, and also involving the left arm. This symptom had occurred on previous occasions. It was associated with a feeling of constriction in the lower sternal region. The legs felt heavy, but were not actually painful, and during the attack the dyspnœa and cyanosis were accentuated. All pulses were palpable in the arms and legs, but that in the dorsalis pedis was very feeble. Catheterization again relieved her symptoms and on the following day her condition had returned to normal. On December 1, she had another similar attack with paræsthesia in the lower part of the body. This time catheterization and morphia gave only incomplete relief. Her condition progressively deteriorated and she died three days later.

The weight of the heart post-mortem was 600 g. Both right and left ventricles were greatly

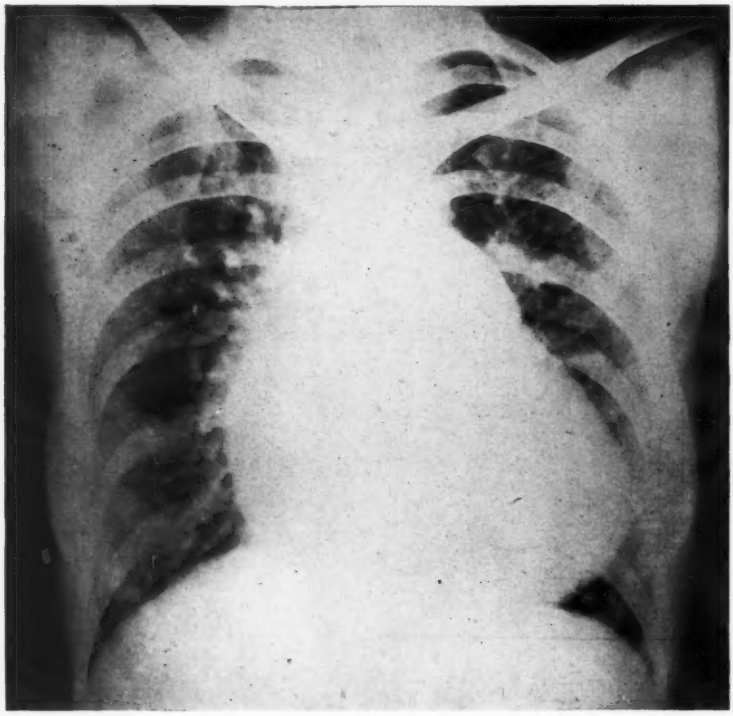

FIG. 5.—Radiogram Case 24, showing a globular heart with general enlargement, but no rib notching.

FIG. 6.—Autopsy specimen Case 24. Aorta, pulmonary artery, and patent ductus arteriosus.

hypertrophied but their cavities were not dilated. The right auricle was hypertrophied but the left auricle appeared normal. The ductus arteriosus was widely patent (Fig. 6). The diameter of the aorta at its origin was normal, but at the point of coarctation between the left subclavian and the ductus it would barely admit a pencil.

Coarctation had not been suspected in this case, though the peculiar paræsthesia in the legs should have aroused our suspicion. Since then in every case of patent ductus I have looked for evidence of coarctation, but hitherto I have found it only once.

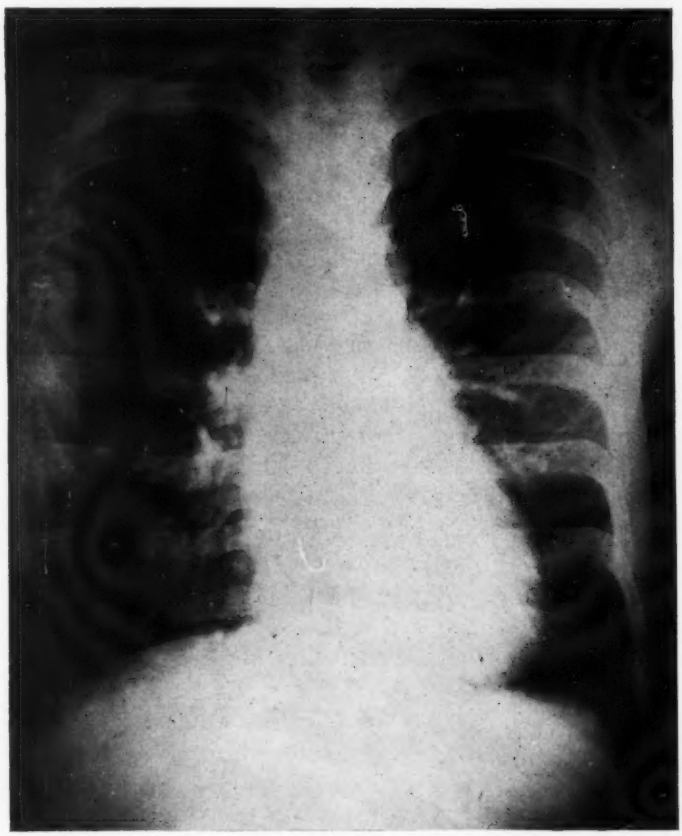

FIG. 7.—Radiogram Case 23 with coarctation and patent ductus arteriosus.

Case 23. A municipal civil servant, aged 27, consulted me because he had been rejected for another post on account of a cardiac murmur. It was the typical machinery murmur of patent ductus. The blood pressure in the arm was 165/80, but the systolic pressure in the dorsalis pedis was only 115. I, therefore, suspected the possibility of coarctation. There were no pulsating arteries on the back or front of the chest and radiography showed no rib notching, but it did show a double prominence in the region of the aortic knuckle (Fig. 7) and on screening it was obvious that the upper knob pulsated violently whereas the pulsation in the lower knob was feeble, the former being proximal and the latter distal to the coarctation.

Case 18. A boy, aged 11, was seen in consultation in September 1936. He had been a promising

athlete for his age and very fit until taken ill at school in July with a pain in the left thigh. Three weeks later he was admitted to a nursing home with a swinging temperature and an enlarged spleen. From August 10 until I saw him the temperature had been normal, but on September 8 he complained of a pain in the left chest and his pulse rate increased from 80 to 116 and subsequently remained rapid.

He had a systolic murmur both at the apex and at the base of the heart. The murmur was also clearly audible on the back of the chest. The blood pressure was 140/90. The spleen was easily palpable and he was considered to be suffering from subacute infective endocarditis. Progress was satisfactory till May 1937 when again, after a motor ride, his temperature rose to 99·4° F. and for a few days he had epistaxis. Subsequently, from time to time, he had pains in the chest, foot, shoulder, and other places, each associated with a rise of temperature.

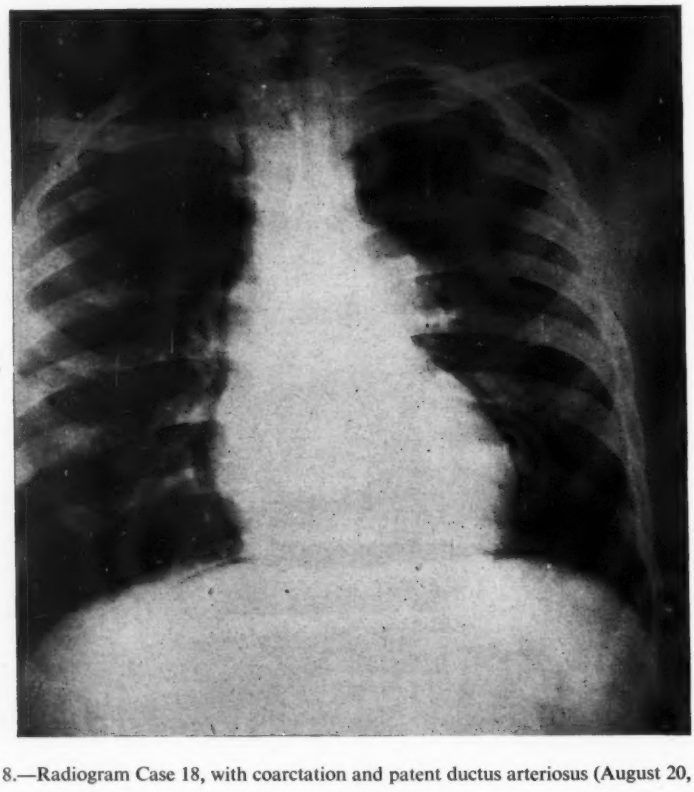

FIG. 8.—Radiogram Case 18, with coarctation and patent ductus arteriosus (August 20, 1937).

He was admitted to my ward on August 11, 1937, and it was then found that no pulsation could be felt in the femoral arteries. X-ray examination of the chest (Fig. 8) by Dr. Twining showed enlargement of the blind end of the descending aorta and enlargement of the pulmonary conus, but no rib notching. Dr. Twining suggested that the radiograms probably indicated coarctation of the aorta associated with patent ductus. Blood culture yielded a profuse growth of *Streptococcus viridans*. This was repeated and confirmed. He was treated with prontosil, but without benefit. On September 18 he developed a dry cough and the air entry in the left lung was found to be diminished. X-ray examination on September 25 showed partial collapse of the left lower lobe and on October 13 complete collapse of the left lung (Fig. 9). The pulmonary complications in this case suggested that the infection involved the ductus as well as the aortic valve.

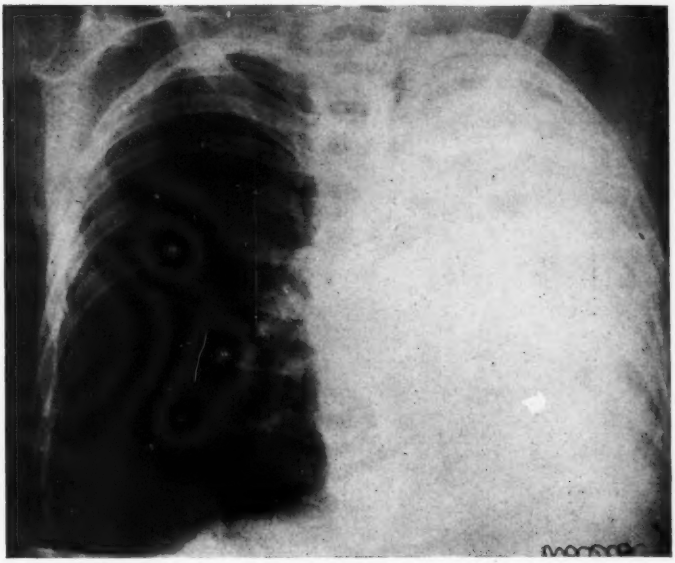

FIG. 9.—Radiogram Case 18, showing collapse of left lung (October 13, 1937).

PROGNOSIS

The number of cases in my series is too small to enable me to draw any firm conclusions regarding prognosis, but certain general deductions appear to be justified. In May, 1945, 10 of my patients were over 30, while 16 were under 30 years of age. Of the latter 3 have been lost sight of. In the older group 4 are dead, in the younger group 6. Of the 4 fatal cases in the older group 3 lived to over 50 years of age and in 2 of these death was not attributable to the coarctation, 1 died of carcinoma of the stomach and the other of lobar pneumonia. Of the remaining 6 patients in this group 5 are not merely alive but free from symptoms. One woman (Case 26) has passed safely through two pregnancies, one man (Case 4) is in a clerical post, and the other 4 all indulge in strenuous physical work. Symptoms dated from childhood in 4 of the 6 fatal cases in the younger group.

It would appear, therefore, that patients whose symptoms date from childhood are unlikely to reach the age of 30, whereas in those who are free from symptoms until the age of 30 the further expectation of life is much more favourable: they have passed safely through the hazards of the third decade.

To the two groups considered above there must be added a third with which I am not concerned in this paper, since young children do not figure in my series. Sixteen of the 28 patients in Evans's (1933) series died in infancy and in 15 of these the coarctation was associated with a patent ductus (see Table I).

Of 82 cases of coarctation collected by Abbott, in which death occurred within the first year, 50 exhibited some major congenital anomaly such as bilocular or trilocular heart, transposition of the arterial trunks, or pulmonary atresia. In the great majority of cases in which death occurs in infancy the coarctation is of the " infantile " type. These cases are of more interest to the embryologist than to the clinician.

It is interesting to compare the expectation of life in my series with that in the series of cases collected by Maude Abbott. Of her 200 cases, 103 (51 per cent) died before the age of 30 and a further 45, making a total of 148 (74 per cent) before the age of 40. In round figures, therefore, half her cases died before 30 and another quarter before 40. Thus between the

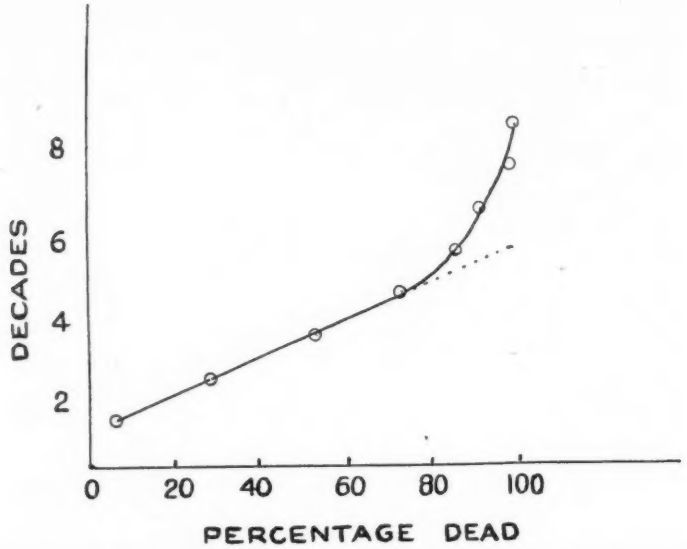

FIG. 10.—Graph showing age and mortality of coarctation of the aorta from Maude Abbott's series.

ages of 10 and 40 there is practically a linear relation between age and death-rate (Fig. 10). Had this been continued after 40, as shown by the interrupted line, all Abbott's cases would have been dead by the age of 50; but after 40, the death-rate tends to fall off, for in patients who reach 40 the coarctation often causes little serious disability, survival for a considerable period of years is not unlikely, and death not infrequently is due to some cause unconnected with the coarctation.

Blackford's figures are very similar to Abbott's. Of 180 cases over 5 years of age, 76 (42 per cent) died between the ages of 16 and 30 and 36 (20 per cent) between 30 and 40. Blackford states that many of these were young athletes who died during or shortly after exercise.

Cause of Death

The cause of death in the 10 fatal cases in my series is shown in Table VIII. Four died of congestive heart failure, 2 of subacute infective endocarditis, and 1 of each of the following conditions, septicæmia, subarachnoid hæmorrhage, carcinoma of the stomach, and lobar pneumonia.

Deaths from congestive heart failure occurred at the ages of 11, 23, 36, and 52. The other fatal cases fall in two well-defined age groups. The three patients who died of cardiovascular causes and the one who died of septicæmia were all under 30, whereas the two who died of

TABLE VIII

CAUSE OF DEATH (BRAMWELL'S SERIES)

Case No.	Age at death	Cause of death	Remarks
1	11	Congestive heart failure	Subaortic stenosis
18	12	Infective endocarditis	Patent ductus
2	23	Infective endocarditis	
15	23	Septicæmia	
24	23	Congestive heart failure	Patent ductus
8	27	Subarachnoid hæmorrhage	
9	36	Congestive heart failure	Two pregnancies Auricular fibrillation
3	52	Congestive heart failure	
5	52	Carcinoma stomach	
6	62	Lobar pneumonia	Auricular fibrillation

causes unconnected with their coarctation were both over 50. This suggests that in patients who survive the hazards of the first three decades the chief danger of coarctation is congestive heart failure.

Subacute infective endocarditis is a well-known complication of congenital heart disease, but the risk of subarachnoid hæmorrhage from rupture of a cerebral aneurysm has not received adequate recognition. Abbott believed that, in young subjects without history of trauma or infection, spontaneous subarachnoid cerebral hæmorrhage was usually due to a ruptured cerebral aneurysm of congenital origin. This was shown at autopsy to be the cause of death in 5 of her cases and she pointed out that the early age of the patients, the large collateral circulation, and the history of repeated small cerebral hæmorrhages suggested that the same was probably true of the other 13 cases of spontaneous cerebral hæmorrhage in which no aneurysm was actually demonstrated.

TABLE IX

CAUSE OF DEATH (ABBOTT AND BLACKFORD)

	Abbott	Blackford
Rupture of heart or aorta	44	38
Myocytic endarteritis of aorta	10	—
Cerebral lesion	24	25
Gradual heart failure	60	68
Sudden heart failure	17	16
Total deaths from cardiovascular causes	155	147
Total number of cases in series	200	196

Maude Abbott and Blackford both found that death was due to cardiovascular causes in over 70 per cent of the cases which they analysed (Table IX). My small series differs from those of Abbott and Blackford in that in no case was death due to rupture of the aorta, a complication that proved fatal in about 20 per cent of their cases. Three of Lewis's cases (Table X) died suddenly at the age of 31, 42, and 49, respectively, but in none of these was the cause of death determined, although in one a post-mortem examination was performed.

An associated congenital abnormality that appears important as a predisposing cause of death is a bicuspid aortic valve. This abnormality not only renders the patient more liable to subacute infective endocarditis but is frequently associated with a congenital weakness of

the aortic wall. A bicuspid aortic valve was present in 22 per cent of the cases in Abbott's series and in over 50 per cent of those in which death was due to spontaneous rupture of the aorta.

An aortic diastolic murmur was detected in only 4 of my patients (Cases 1, 3, 6, and 15). Perlman, on the other hand, reported a diastolic murmur in 10 of his 13 cases. This very high incidence is difficult to explain unless he applied the term " diastolic " to what other workers call a " late systolic " murmur.

Hazards of Coarctation

Bonnet (1903) maintained that fully compensated obstruction of the thoracic aorta made no extra demand on the cardiac reserve, and that hypertrophy of the heart was never present in uncomplicated cases. Lewis (1933) held the view that prolonged overwork in itself never led to heart failure. Abbott (1928) on the other hand believed that uncomplicated coarctation did entail cardiac strain which might by itself lead to death from failing compensation. She quotes a large number of observations in support of this hypothesis, and she found that cardiac hypertrophy was present in 75 per cent of the 200 cases she reviewed.

A detailed statement concerning cardiac enlargement in my own cases will be given in a later paper dealing with the radiology of coarctation. Here let it suffice to say that gross cardiac enlargement was present in only 4 of my 26 cases: in 3 of these (Cases 1, 3, and 6) it was associated with aortic incompetence and in the fourth (Case 24) with a freely patent ductus.

Case 2 is of particular interest in that we were able to compare the cardio-thoracic ratio at the age of 11 and 21. No alteration had occurred. Lewis (1933) reported little if any increase in heart size in those of his cases that were under observation for several years. These were older men: in my case there was no relative increase in heart size over the period of active growth.

My own observations lead me to believe that coarctation of the aorta does impose an additional load on the heart which entails a corresponding reduction in the cardiac reserve, but that, in the adult type of coarctation, this alone is not sufficient seriously to embarrass the heart during the first half of life, nor to render it incapable of meeting its everyday commitments. When coarctation is not complicated by the presence of some other heart lesion, symptoms of circulatory insufficiency are not likely to supervene unless the heart muscle be weakened by intercurrent infection, or an additional burden be imposed upon the heart by severe physical strain, in which case a progressive deterioration in health may ensue.

Not infrequently patients date their symptoms from some intercurrent infection which appears permanently to have upset the equilibrium. This is clearly illustrated by Lewis's series of cases of coarctation amongst pensioners from the First World War. These men had been invalided out of the army on account of cardiovascular symptoms and it is interesting to note the various conditions that were responsible for their breakdown. In three (Table X) symptoms of circulatory insufficiency developed following an attack of malaria. One (Case 3) developed symptoms at the age of 19 following an attack of P.U.O. which from Lewis's description sounds like trench fever. In a fifth (Case 6) a man of 27, who had served three years in the army, symptoms followed a foot infection. Thus in 5 of Lewis's 8 cases the onset of symptoms was attributable to intercurrent infection. There is, however, little evidence that a progressive cardiovascular deterioration occurred as the result of such infection since all five men survived for more than 10 and one for 24 years. This patient was 63 at the time Lewis's paper was published and subsequently attained the age of 73.

I am indebted to Dr. E. E. Pochin for the further history of this remarkable case, who was under treatment by Sir Thomas Lewis in October 1942 with increasing breathlessness over the

TABLE X

LEWIS'S CASES FROM THE 1914–18 WAR

Case	Predisposing cause	Age first symptom	Remarks	Duration (years)	Age at death	Cause of death
1	3 months' training ..	19	Previously active	12	31	" Sudden "
6	Foot infection ..	27	3 years' service	15	42	" Sudden "
7	Malaria	33		10	43	Infective endocarditis C.H.F. (P.M.)
8	After 4 months' France	41	Previously reserve	8	49	" Sudden " (P.M.)
4	Cycle accident ..	40	Detached retina	12	52	C.H.F. auricular fibrillation
5	Malaria	49	Rejoined 1914 aged 47	12	61	Acute pneumonia
2	Malaria	49	Enlisted 46 R.F.A. 3 yrs. foreign service	14+	—	Living 63*
3	P.U.O.	19	14 months front line, football	17+	—	Living 36

* Died 1944, aged 73.

previous twelve months and with several attacks of loss of consciousness during the preceding few weeks. He then could not walk more than 200 yards without having to stop owing to breathlessness and was made breathless by one flight of stairs. The attacks of unconsciousness occurred shortly after waking and were continued in hospital where he was found to have heart block. The degree of block was variable, some records showing a long P–R interval with a 1:1 ventricular response; most showing 2:1 block with a ventricular rate of about 44 with some failures of ventricular response and some extrasystoles; while some records showed complete heart block.

He had at this time 4 cm. of venous congestion, the cardiac apex beat was 15 cm. to the left in the fifth space, the right border of dullness being 4 cm. to the right of the mid-line. The blood pressure was 200/120 in the arms and 80/60 in the legs. On treatment with ephedrine his Stokes-Adams attacks ceased and his heart rhythm became regular at a rate of about 80, but he still showed alternation of the pulse and gallop rhythm. He was seen at intervals until October 1944 when he died, out of hospital. No details of his form of death are available, but a post-mortem was obtained and the specimen is now in the Pathological Department of University College Hospital.

Severe physical strain is another hazard to which these patients are liable to be exposed, for as Abbott points out the majority are males and many are of an athletic, muscular build. Blackford (1928) states that in many cases sudden death from rupture of the aorta has occurred during or immediately after athletic exertion.

Pregnancy and Coarctation

A correct appreciation of the dangers of childbirth in women with coarctation is important, since grave complications are liable to develop unexpectedly during the second stage of labour. Two* of the patients in my series have been under observation during pregnancy.

Case 26. A woman aged 37 was referred to my clinic in the fourth month of her second pregnancy on account of a history of mitral stenosis. She was delivered by Cæsarean section in August 1945 and when last seen in August 1946 was well except for slight breathlessness on exertion. Up to the age of 20, when she first consulted a doctor on account of breathlessness when cycling and œdema of

* Two other cases seen since May 1945 have been successfully delivered by Cæsarean section.

the ankles, she had been perfectly fit. A heart murmur was discovered at that time. This was wrongly attributed to mitral stenosis and she was accordingly kept in bed for six weeks. Subsequently, until her marriage at the age of 24, she worked as a machinist and lost little time off work through ill health, but strenuous exertion made her breathless. Convalescence following her first confinement—a forceps delivery at the age of 29—was prolonged and she was in bed for six weeks, but from then onwards she enjoyed good health until she again became pregnant. Apart from her illness at the age of 20, which appeared to be attributable to over-exertion, this woman had little in the way of symptoms except during her two pregnancies.

Case 9.—A primigravida, aged 31, was admitted to St. Mary's Hospital, Manchester, with a view of Cæsarean section for contracted pelvis, and was referred to my clinic in March 1933 on account of high blood pressure. She had been unaware of any heart trouble up to the fourth month of pregnancy when she had noticed some shortness of breath and palpitation. For sixteen years before her marriage at the age of 29, she had worked hard on a farm where her daily routine included heavy lifting and scrubbing.

She was successfully delivered by Cæsarean section in April 1933. Six weeks later she developed a severe hypochromic anæmia which responded well to treatment and she then remained free from symptoms until November 1935 when she began to complain of lassitude, palpitation, and præcordial pain on exertion. On examination it was found that she was again pregnant and had developed auricular fibrillation. In May 1936 she had a complete abortion from which she made a good recovery, but subsequently she developed congestive heart failure from which she died in May 1938. This case has already been fully reported (Bramwell and Longson, 1938).

A case reported by Walker (1943) presented some similarity to the one described above. She also was a farmer's wife, 31 years of age, but before marriage her activities had been considerably restricted. She remained fit throughout pregnancy and tolerated the first stage of labour well, but became acutely distressed and breathless following rupture of the membranes. She was delivered by forceps and convalescence was uneventful.

The alarming complications that may develop unexpectedly during labour are illustrated by a case reported by Billinghurst (1943). His patient, a healthy and athletic primipara of 23, who had no symptoms during pregnancy, fainted at the onset of the second stage of labour and died suddenly the day after delivery from rupture of the aorta.

TABLE XI

JENSEN'S CASES OF COARCTATION ASSOCIATED WITH PREGNANCY

Author	Date	Age	No. of children	Remarks
Leudet	1858	37	4	Died from rupture of aneurysm just beyond coarctation
Kreigh	1878	28	2	Died following stroke in 9th month of her 3rd pregnancy
Fawcett ..	1905	45	9	Died of congestive heart failure 14 days after induction of premature labour
Abbott	1915	38	1	Died of congestive heart failure some years after confinement
Katz	1921	25	1	Died on rupture of the aorta near the end of 2nd pregnancy
Strassmann ..	1922	56	7	Found dead in bed
Strayhorn ..	1937	26	0	Successfully delivered by Cæsarean section

In 4 of the 7 cases collected by Jensen (1938) (Table XI) death occurred either during pregnancy or shortly after delivery from causes directly related to the coarctation : but one of these women had survived eight previous pregnancies and another lived to the age of 56 after having had seven children.

Summary and Conclusions

Twenty-six cases of coarctation of the aorta are reported. In 20 the diagnosis was based on clinical evidence, in 5 it was made by the radiologist, and in 1 the lesion was discovered post-mortem.

The classification, clinical manifestations, and prognosis of the condition are discussed and the following conclusions are reached.

Coarctation of the aorta is apt to escape recognition, unless the possibility of the condition be continually kept in mind. Many of Lewis's cases were under observation for years before they were correctly diagnosed. When associated with a patent ductus or with aortic incompetence, coarctation is especially liable to be overlooked.

Clinically the diagnosis is based on the finding of high systolic blood pressure in the upper limbs associated with low pressure in the lower limbs, pulsating arteries on the back or front of the chest, excessive arterial pulsation at the root of the neck, and a late systolic murmur of abnormal distribution. The most important radiological manifestations are rib notching and occasionally a double aortic knuckle. Direct demonstration of the coarctation is rarely possible. Diagnosis is most difficult when the ductus is patent, for then there may be no collateral circulation and no notching of the ribs.

In many cases, symptoms first appear following some intercurrent infection or physical strain. Dyspnœa, palpitation, and fatigue are the most common complaints. Pain in the trunk and arms may be due to pressure on nerves by the dilated arteries participating in the collateral circulation. The spinal anastomosis is of importance in this connection.

Despite a deceptively good exercise tolerance, a sudden strain may prove fatal even in the prime of life: these patients are living dangerously. It is accordingly wise to limit their activity. Women with coarctation should be delivered by Cæsarean section.

In coarctation of the aorta fatal complications are so liable to develop unexpectedly that prognosis is extremely uncertain: a patient who appears to be in robust health one day may be dead the next.

Patients in whom symptoms date from childhood rarely live to 30, whereas those who surmount the hazards of the first three decades may suffer little disability from their coarctation. The efficiency with which the circulation may be maintained year after year, in spite of the increased load due to high blood pressure, is remarkable.

I am indebted to Dr. A. Morgan Jones for his help in the investigation of these cases, to Dr. E. Duff Gray and the late Dr. E. W. Twining for the radiograms, to Dr. W. Susman for the pathological observations in Case 24, to Dr. E. E. Pochin for particulars of Lewis's case, to Dr. William Evans and the Oxford University Press for permission to reproduce Fig. 1–3, and to other colleagues for referring cases to me.

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APPENDIX

Two patients in this series who were alive in May 1945 have since died. Their subsequent history and the post-mortem findings were as follows.

Case 13. This man was admitted to the Bolton Royal Infirmary on 15/10/45 suffering from subarachnoid hæmorrhage from which he made an uneventful recovery. He was readmitted on 9/12/46 following a severe hæmoptysis. His blood pressure then was 130/70. During the ensuing week three further hæmoptyses occurred, and he died on 16/12/46.

I am indebted to Dr. Horace Jackson for the further clinical history in this case and for the following report on the post-mortem examination. There was a cavity filled with fresh blood clot in the lower lobe of the right lung and the surrounding tissue was saturated with blood. The hæmorrhage appeared to have resulted from rupture of a fairly large vessel, but there was no clear evidence of an aneurysm. There was no tuberculosis. Just distal to the origin of the left subclavian artery, at the point of insertion of the ductus, which was closed, the aorta was narrowed, but not completely occluded (Fig. 11 on p. 126). It admitted a probe 0·2 cm. in diameter. The internal mammary vessels were very large. Examination of the brain revealed an aneurysm about 1 cm. in diameter on the circle of Willis. The surrounding brain showed staining from an old hæmorrhage—probably that from which the patient suffered in 1945.

Case 20. This young man kept well until April 1946 when, after rowing, he had an attack of sweating, and for three days was febrile, complaining of pain in the right thigh and right foot. Four weeks later he had another febrile attack, again after rowing. He was then seen by Dr. D. Rhodes Allison who diagnosed subacute bacterial endocarditis and admitted him to a private ward at the Manchester Royal Infirmary on 7/6/46. I am indebted to Dr. Allison for the opportunity of seeing this patient at that time and for the further particulars of his illness. He was treated with penicillin and progress was satisfactory until 27/6/46 when he complained of pain in the chest. Two days later he vomited copiously and from that time his condition steadily deteriorated. On 2/7/46 he collapsed suddenly and died.

Post-mortem examination by Dr. F. A. Langley showed a narrowing of the aorta just proximal to the insertion of the ductus arteriosus which was closed, the lumen of the aorta at this point being less than 0·5 cm. in diameter, whereas that of the descending aorta was 1·0 cm. in diameter (Fig. 12 on p. 127.) Beyond the coarctation, for a distance of 3 cm. the wall of the aorta was much thickened and roughened and small vegetations were present. The internal mammary artery and its branches were very large. They did not directly anastomose with the deep epigastric artery but broke up into small muscular vessels in the rectus abdominis just above the umbilicus. The heart weighed 700 g., the left ventricle being greatly dilated. The interventricular septum was displaced to the right reducing thereby the capacity of the body of the right ventricle (Bernheim's syndrome). The conus of the right ventricle was dilated. The right auricle was dilated and its wall somewhat thickened. The left auricle appeared normal. The aortic valve was bicuspid, both coronary arteries arising from the anterior sinus of Valsalva; the anterior cusp was thickened and on it there were a few small vegetations; the posterior cusp had a large vegetation covering its ventricular surface. The coronary arteries appeared normal.

I am indebted to the Department of Pathology of the University of Manchester for the photographs of the post-mortem specimens.

FIG. 11.—Specimen of coarctation from Case 13.

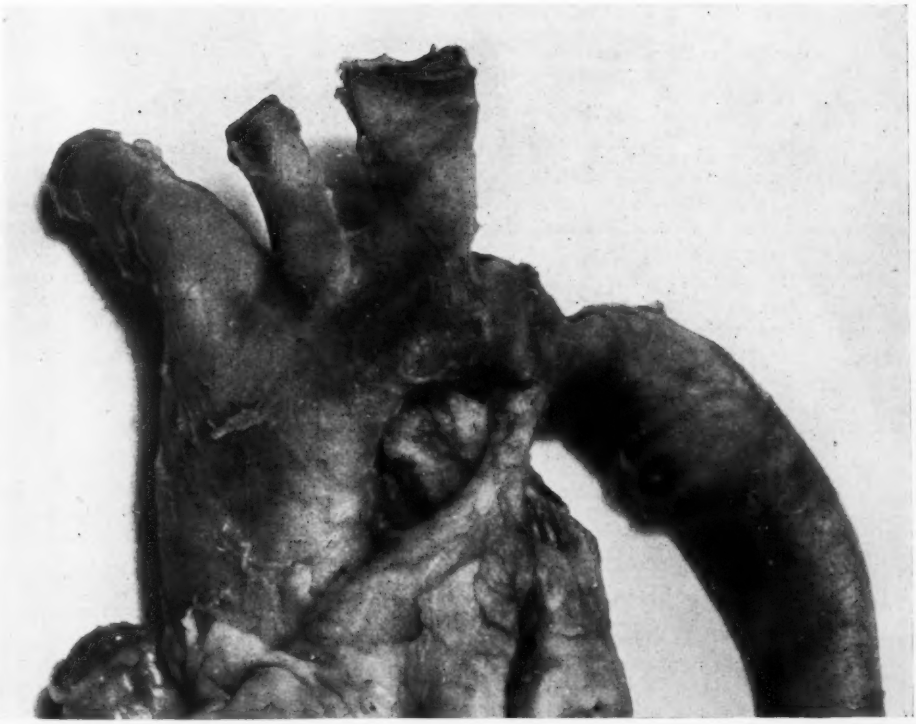

FIG. 12.—Specimen of coarctation from Case 20.

THE HEART IN TOXÆMIA OF PREGNANCY

BY

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Although acute pulmonary œdema is a recognized complication of toxæmia of pregnancy, its mechanism is incompletely understood. In some of the reported cases the clinical picture was similar to that of cardiac asthma and the cause of the pulmonary œdema was thought to be left ventricular failure. Detailed studies of the heart in toxæmia of pregnancy, however, have been few, and reports showing that toxæmia of pregnancy may be associated with myocardial damage are not many. Some of the cases of acute heart failure reported in late pregnancy and in the early puerperium in patients who had no signs of antecedent cardiovascular disease may have been instances of toxæmia with associated myocardial damage. Thus, Blacker (1907) and later Campbell (1923) noticed the occurrence of heart failure during and after pregnancy, and in the absence of a valvular lesion they regarded myocardial disease as the possible cause for it. Herrmann and King (1930) called attention to " significant types of cardiac failure occurring in pregnant patients with non-valvular heart disease." Toxæmia was apparently present in some of their patients.

Eufinger and Molz (1936) undertook a cardiographic study of 23 cases of toxæmia of pregnancy, but were unable to demonstrate myocardial disease. Gouley, McMillan, and Bellett (1937) observed heart failure and T wave changes in the cardiogram shortly after delivery. Some of their patients died, and the histological examination showed focal myocardial necrosis; the coronary arteries were found to be normal. In two of the cases the blood pressure was raised, but in only one surviving case was toxæmia described by the authors. Teel, Reid, and Hertig (1937) reported 6 cases of toxæmia of pregnancy complicated by cardiac asthma and pulmonary œdema; one came to autopsy, and the histological sections of the heart showed œdema of the stroma and occasional cellular infiltration, with slight subendocardial fibrosis and occasional thickening of the internal elastic membrane of the smaller coronary branches. They concluded that the œdema and the leucocytic infiltration of the myocardial tissue were consistent with an acute process that could have interfered with the cardiac function. Hull and Hidden (1938), reporting on the occurrence of post-partum heart failure, mentioned toxæmia of pregnancy and nutritional deficiency as possible ætiological factors; hypertension with a systolic pressure above 150, was present in one third of their cases. Thomson, Cohen, and Hamilton (1938) studied chest lead cardiograms in pregnancy, including normal subjects and patients with heart disease or toxæmia, and found that an upright T wave was usual in toxæmic patients (they used the old method of recording chest leads, according to which the T wave was normally inverted): the R wave was entirely absent or less than 2 mm. in some of the toxæmic and cardiac patients, but never in the normal cases. Bradford (1939) stressed the danger of cardiac decompensation in acute pre-eclampsia. According to Dexter and Weiss (1941) and Dexter *et al.* (1943), the heart is usually normal when toxæmia is mild, but severe toxæmia with generalized œdema is frequently associated with

heart failure. They found changes in 2 of 12 cardiograms, and in both the changes appeared in the post-partum period, on the 6th and 9th day respectively: in the second the cardiogram was normal 7 days before term when signs of heart failure were present, and it became abnormal later when the failure had subsided. Dieckmann (1942) stated that patients with mild toxæmia rarely showed evidence of cardiac damage, but those with severe pre-eclampsia and eclampsia usually had tachycardia and occasionally developed heart failure. Recently Wallace, Katz, Langendorf, and Buxbaum (1946) studied the cardiogram in 12 cases of pregnancy toxæmia and found changes similar to those seen in anterior myocardial infarction in 2, both of which had heart failure; 4 showed alterations in the T wave and prolonged A–V conduction, but no clinical evidence of heart failure; and in the remaining 6 there was neither clinical nor cardiographic evidence of cardiac involvement.

Personal Observations

The present paper is based on the observations made in 19 unselected cases of toxæmia of pregnancy, delivered in the Department of Obstetrics of the Newcastle General Hospital. Although the difficulty of assessing the severity of the toxæmic state is fully recognized, an attempt has been made to classify the cases for the purposes of this study. The majority were classified as severe, the criteria being subjective symptoms, such as headache, vomiting, and visual disturbance, and height of blood pressure, œdema, albuminuria, and the occurrence of eclamptic fits. All the " severe " cases had a blood pressure of more than 160/100, in addition to other symptoms and signs of toxæmia, except one with a blood pressure of 130/95, classified as severe because of eclamptic convulsions.

Clinical and cardiographic studies were made in all and, in addition, radioscopic examination in 9 cases. The cardiovascular findings are summarized in Table I. A total of 7 cases were thought to show significant clinical and/or cardiographic changes. Left ventricular failure was observed in 3 (Cases 1, 13, and 19), and the first of these also showed T wave changes similar to those seen in anterior myocardial infarction. Significant cardiographic changes were seen in 5 (Cases 1, 8, 11, 17, and 18), these changes consisting of transient alterations of the T waves usually in both standard and chest leads (Fig. 1–5). Cardiographic changes of doubtful significance were observed in 6 others. In the remaining 8 the cardiograms were within normal limits. Sinus tachycardia was frequent and extrasystoles were observed in 2 (Cases 17 and 19).

Case 1, para 3, aged 36. Admitted on 17/7/42 with œdema of the legs, albuminuria, and a B.P. of 185/120. She had a normal labour and was delivered on 24/7/42. Three days later she developed acute pulmonary œdema. There was marked tachycardia, triple rhythm, and slight papillœdema. The cardiogram (Fig. 1A) showed inverted T waves in the limb leads. The clinical condition gradually improved, the triple rhythm disappeared, and on 18/8/42 she had no signs of cardiac failure, no albuminuria, and no œdema. Her B.P. was 145/95. However, the cardiogram (Fig. 1B) was still very abnormal, showing inverted T wave in leads I, II, and IV. Radioscopic examination showed a normal-sized heart. On 4/9/42 the B.P. came down to 140/90. Repeated cardiograms were done, and a gradual increase in the voltage of the T waves was noted. The tracing taken on 19/11/42 (Fig. 1C) showed a complete return to normal. The patient was seen three months later when she was complaining of headaches. Her heart was normal clinically, radiologically, and cardiographically, but her B.P. was 170/100 and the retinal vessels were thought to be slightly thickened.

Case 8, para 0, aged 21. Admitted on 22/9/44 complaining of headaches, dimness of vision, and eclamptic fits of three days' duration. She was delivered on 25/9/44. The highest blood pressure was recorded on the second post-partum day when it was 180/110. The first cardiogram (Fig. 2A), taken on 27/9/44, showed T wave changes and small R wave in lead CR_8. Another taken 7 days later showed improvement (Fig. 2B). Her B.P. came down to 120/85. The albuminuria and œdema had disappeared, and radioscopic examination showed a normal-sized heart. The patient was seen

again in March 1945, when her B.P. was 120/80 and the clinical, radiological, and cardiographic findings were also normal.

Case 11, para 10, aged 38. Admitted on 6/10/44 with marked œdema of the legs, albuminuria, and a B.P. of 200/140. She was delivered on 12/10/44 by Cæsarean section. On 14/10/44 her B.P. was 160/100 and there was a slight papillœdema. Clinically, the heart was normal. However, a cardiogram taken on the same day (Fig. 3A) showed flat T wave in leads II and IVR, and inverted T wave in leads III and CR_2; the initial deflection was absent in CR_2; and the electrical systole was prolonged. Fig. 3B, taken on 18/10/44, showed improvement. On 25/10/44 the cardiogram still showed an absent R wave in lead CR_2, but otherwise it was normal (Fig. 3C). On radioscopic examination, the heart was normal in size. The optic discs looked normal. There was no œdema and no albuminuria; the B.P., however, remained 160/100.

Case 13, aged 34. Admitted on 15/12/44 with œdema of legs, albuminuria, and a B.P. of 160/100. She was delivered on 24/12/44. On 6/1/45 she was found to have tachycardia, triple rhythm, and evidences of pulmonary congestion. The retinal vessels looked normal, and the B.P. was 150/100.

TABLE I

CARDIOVASCULAR FINDINGS IN TOXÆMIA OF PREGNANCY

Case No.	Age	Toxæmia	B.P. (maximum)	Heart			Electro-cardiogram	Remarks
				Rate	Sounds	Size		
1 (Fig. 1)	36	Severe	185/120	140	Triple rhythm	Normal (X-ray)	Inverted TI, TII, TIV	Left ventricular failure
2	29	Mild	160/100	88	Normal	Normal	Normal	—
3	29	Severe eclampsia	170/100	80	Normal	Normal (X-ray)	Low TII. Inverted TIII. Low TIV	—
4	34	Severe	180/130	60	Normal	Normal	Normal	—
5	25	Severe	190/130	100	Normal	Normal	Normal	—
6	22	Severe eclampsia	130/95	130	Normal	Normal	Normal	—
7	32	Severe	160/110	120	Normal	Normal	Low TI. Isoelectric TIV	—
8 (Fig. 2)	21	Severe eclampsia	180/110	80	Normal	Normal (X-ray)	Isoelectric TI. Inverted TIV	—
9	29	Severe	180/110	90	Normal. Apical S.M.	Normal	Depressed S–TIV. Low TIV. RIV <2 mm.	— —
10	23	Mild	160/100	70	Normal	Normal	Normal	—
11 (Fig. 3)	38	Severe	200/140	110	Normal	Normal (X-ray)	Isoelectric TII. Inverted TIII and TIV	? Antecedent hypertension. Cæsarean section
12	23	Mild	160/100	90	Normal	Normal (X-ray)	Low TIV	? Antecedent hypertension. Died of uræmia six months later
13	34	Mild	160/100	100	Triple rhythm	LV+ (X-ray)	Normal	Left ventricular failure; ? antecedent hypertension
14	36	Mild	150/100	70	Normal	Normal	P–R+	—
15	31	Severe	170/105	80	Normal	Normal	Normal	—
16	32	Severe	175/115	90	Normal	Normal	RIV<2 mm.	Delivered by Cæsarean section
17 (Fig. 4)	21	Severe eclampsia	210/140	130	Normal	Normal (X-ray)	Low TI. Inverted TIV. Extrasystoles	Post-partum vascular collapse
18 (Fig. 5)	21	Severe	200/150	100	Normal	Normal (X-ray)	Isoelectric TII. Inverted TIII and TIV	—
19	31	Severe	200/110	100	Triple rhythm	Normal (X-ray)	Normal	Left ventricular failure

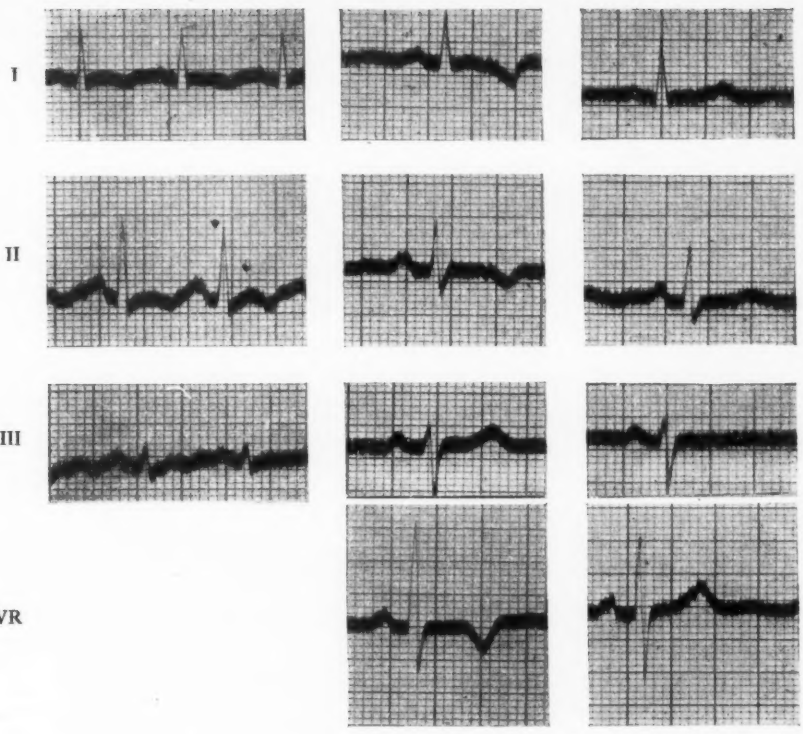

FIG. 1.—Case 1. Toxæmia complicated by left ventricular failure. Delivered on 24/7/42. (A) 27/7/42; abnormal T waves. (B) 18/8/42; deeply inverted T wave in leads I, II, and IV. (C) 19/11/42; normal tracing.

A cardiogram showed left axis deviation and normal complexes. The radioscopic examination showed slight enlargement of the left ventricle. The patient made a good recovery, the triple rhythm and the pulmonary congestion had disappeared. She was discharged and a follow-up was, unfortunately, impossible.

Case 17, para 0, aged 21. Admitted on 9/4/46 with eclampsia, albuminuria, and œdema of legs and face. Her B.P. was 210/140. She was delivered on the same day. Twelve hours after delivery she showed evidences of a vascular collapse, the heart rate being 130 a minute and the B.P. 90/70. The patient had only a very slight loss of blood, which could not account for the collapse. She was given blood and plasma transfusions and she gradually improved. On 11/4/46 her B.P. was 130/90. Fig. 4A showed flat T II and inverted T in leads III and CR_2. There was some improvement in Fig. 4B and C, taken five and nine days later.

Case 18, para 0, aged 21. Admitted on 12/4/46 with severe albuminuria and œdema of legs. The B.P. was 200/150, and there was a slight papillœdema. She was delivered on 16/4/46. Fig. 5A, taken the next day, showed the T waves flat in leads II and IVR, and inverted in leads III and CR_2. Clinically the heart was normal. The B.P. was 170/145, on the same day and on 23/4/46 had fallen to 150/120. The cardiogram (Fig. 5B) showed higher T waves. On 27/4/46 the B.P. was 130/90 and the optic discs looked normal. The cardiogram showed no abnormality (Fig. 5C), and on screen examination the heart was normal in size. Also the œdema and albuminuria had completely cleared up.

Case 19, para 4, aged 31. Admitted on 28/6/46 with severe œdema of the legs. The B.P. was 200/110. On 2/7/46 she suddenly became very dyspnœic, and was found to have tachycardia with triple rhythm and pulmonary congestion. No cardiogram was done. She was delivered on 6/7/46. Following delivery, there was a gradual improvement, and on 18/7/46 the clinical, cardioscopic, and cardiographic findings were normal. Her B.P. was 130/80, and the œdema of the legs had cleared up completely. The patient was seen again a month later, when the cardiovascular system was found to be normal in every respect.

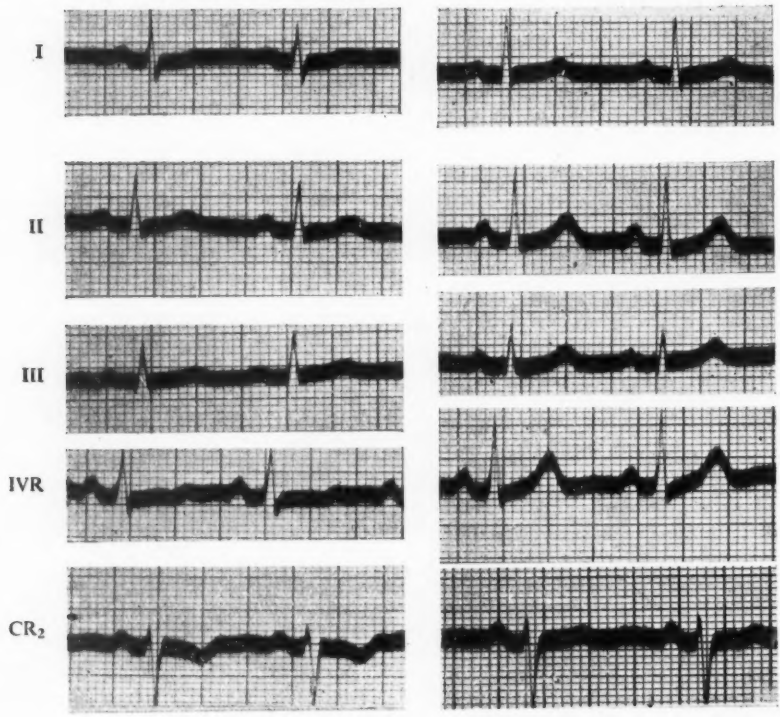

FIG. 2.—Case 8. Eclampsia. Delivered on 25/9/44.
(A) 27/9/44; flat or inverted T waves. (B) 9/10/44; T waves returning to normal.

DISCUSSION

In the present series a total of 7 patients (37 per cent) were thought to have significant changes in the heart: 2 showed clinical changes only, 4 cardiographic changes only, and 1 showed both clinical and cardiographic evidence of cardiac involvement. This incidence of cardiac involvement in toxæmia of pregnancy is somewhat lower than that recently reported by Wallace *et al.* (1946), who found cardiac changes in 6 of 12 cases.

Thomson, Cohen, and Hamilton (1938) observed transient abnormality of the T wave in the chest lead in some of their normal pregnant patients. Wallace *et al.* (1946), found an inverted T wave in lead CF_2 in a pregnant woman whose heart was believed to be normal, and suggested that such inversion of T in the chest lead may occur in normal pregnancy.

As regards our present series, we believe that the cardiographic changes were indicative of myocardial damage in at least 5 cases, because they occurred in both standard and chest leads, and persisted for some time after delivery, so that the alteration in the anatomical position of the heart during pregnancy could be excluded as causative factors. Furthermore, one of us (P. S.) has examined the records of several pregnant women, including patients with normal hearts, with chronic rheumatic heart disease, and with permanent arterial hypertension

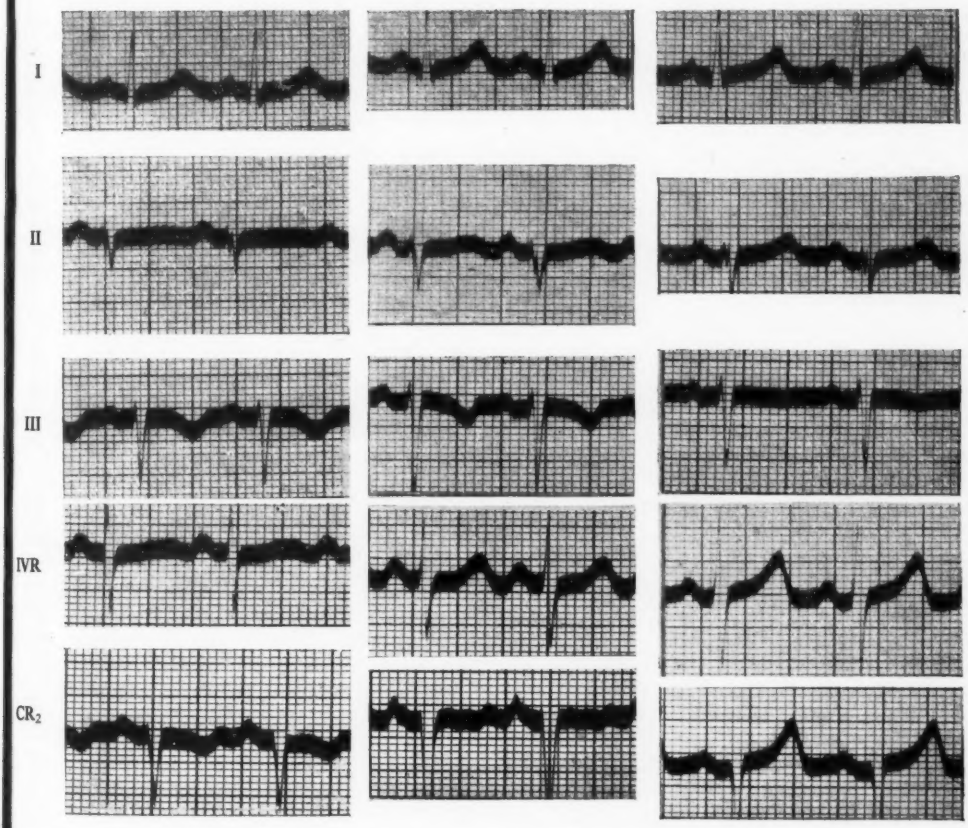

FIG. 3.—Case 11. Probable chronic hypertension with superimposed toxæmia. Delivered by Cæsarean section on 12/10/44.
(A) 14/10/44; definite T wave changes, absent R wave in CR_2, prolonged electrical systole. (B) 18/10/44; T waves getting higher. (C) 25/10/44; still absent R wave in CR_2, otherwise normal tracing.

without superimposed toxæmia, both ante-partum and post-partum, and has not observed a sequence of cardiographic changes similar to those seen in some of the toxæmic patients.

The changes in the heart appear to be temporary, but their duration varies considerably. The changes may not only persist for some time after delivery, but may become greater in the post-partum period. This has been previously stressed by Dexter and Weiss (1941) and Wallace *et al.* (1946), and is also borne out by our own observations.

Although it is highly probable that there is a causal relationship between toxæmia of pregnancy and cardiac damage, it is not quite clear how the latter is brought about. According to Dexter and Weiss (1941) the syndrome of cardiac asthma and pulmonary œdema may be caused by two factors, singly or combined—primary fluid retention in the lung tissue caused by factors specific to toxæmia, and left ventricular failure—and the mechanism of pulmonary

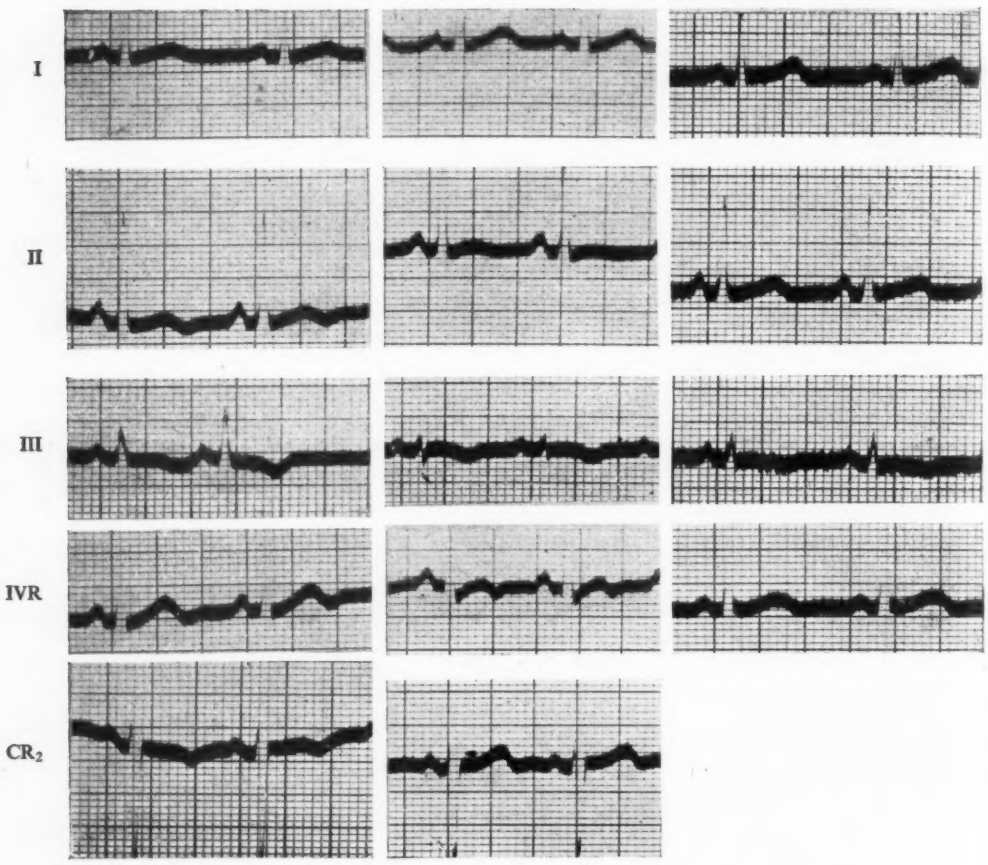

FIG. 4.—Case 17. Eclampsia. Delivered on 9/4/46. Post-partum vascular collapse. (A) 11/4/46; T wave changes, extrasystole in lead III. (B) 16/4/46; T in CR_4 positive, but still abnormal tracing. (C) 20/4/46; T waves returning to normal.

œdema in toxæmia of pregnancy is in many respects similar to that in beri-beri. Although there are some reports suggesting a causal relationship between toxæmia of pregnancy and vitamin B_1 deficiency (Siddall, 1940; King and Ride, 1945), the clinical and especially the cardiographic features of myocardial injury in toxæmia are unlike those seen in beri-beri heart disease.

Dieckmann (1942) found that in pre-eclampsia especially if severe, there is a concentration of blood during the height of the disease and dilution with clinical improvement. According

to him hæmo-concentration places a tremendous strain on the heart because the thickened blood with increased viscosity requires more work by the heart and at the same time favours a decrease in the coronary circulation. Wallace *et al.* (1946) are of the opinion that focal myocardial necrosis, œdema, and infiltration are the essential factors in producing the cardiographic changes and precipitating the heart failure.

While the cardiac failure of the left ventricular type may be in some cases the direct result of the hypertension, it is unlikely that the latter condition is responsible for the cardiographic

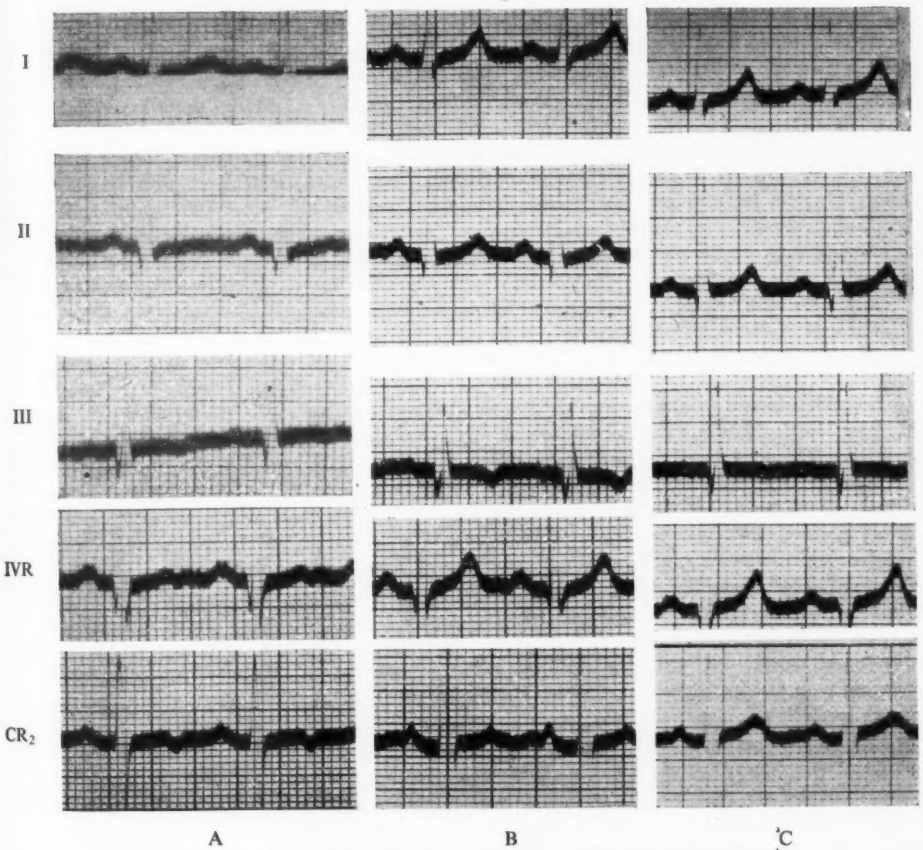

FIG. 5.—Case 18. Severe toxæmia. Delivered on 16/4/46.
(A) 17/4/46; marked T wave changes. (B) 23/4/46; T waves getting higher. (C) 27/4/46; normal tracing.

changes. The rise in the blood pressure in pure toxæmia or in patients with antecedent hypertension and superimposed toxæmia is usually not of sufficient duration to be an ætiological factor. On the other hand, the changes, if any, in persistent hypertension would not be limited to the period of pregnancy and the puerperium. One can assume, therefore, that the cardiographic abnormalities indicate changes in the heart that have a direct bearing on the " toxæmic " state. We have recently had the opportunity of following up a 28-year-old primigravida who had coarctation of the aorta with a blood pressure of 220/130 in the upper

extremities and enlargement of the left ventricle. There was nothing to suggest a superimposed toxæmia. Frequent cardiograms were done, including IVR and CR_2 chest leads, from early pregnancy to the puerperium, and all records were strictly normal.

It would appear from our observations that gross cardiac enlargement is not a feature of pure " toxæmic " cardiac lesion, irrespective of the presence or absence of cardiac failure. Only one of our cases (Case 13) showed enlargement of the left ventricle. It is true that the radioscopic examination in many of our cases was not carried out at the height of the disease; nevertheless, the clinical impression as a rule was that of a normal-sized heart. If gross cardiac enlargement is present, it probably indicates either antecedent hypertension or heart disease not " toxæmic " in origin. There is nothing to suggest that pericardial effusion is present in toxæmia of pregnancy to account for the cardiographic changes or the heart failure.

Toxæmia of pregnancy is an acute vascular disorder and in this respect it closely resembles acute glomerulo-nephritis (Dexter and Weiss, 1941). Cardiac involvement is known to occur in acute nephritis. Ellis (1942) found cardiac impairment in 21 per cent of his cases of acute nephritis, and states that " the picture is that of the left ventricular failure with pulmonary œdema; it is possibly due to involvement of the myocardial vessels in the widespread vascular disorder that we believe to be characteristic of this type of nephritis." Cardiographic changes may also be present in acute nephritis (Langendorf and Pick, 1938), and Wallace *et al.* (1946) pointed out recently that the cardiographic changes observed in toxæmia of pregnancy are similar to those seen occasionally in acute glomerulo-nephritis. Our as yet unpublished observations are in agreement with this view. Wallace *et al.* (1946), however, are inclined to think that while the predominant pathological changes in the heart in acute nephritis result from vascular damage, the changes in toxæmia of pregnancy consist of focal myocardial necrosis. This is supported to a great extent by the available pathological findings (Teel, Reid, and Hertig, 1937; Gouley, McMillan, and Bellett, 1937). On the other hand, it is now well established, both clinically and anatomically, that toxæmia of pregnancy is associated with generalized vascular changes (Bell, 1932; Wagener, 1933; Herrick and Tillman, 1935; Jones, 1937; and Browne, 1944). Wagener (1933) states that in "toxæmia of pregnancy —just as in glomerulo-nephritis—the presence of lesions of the retinal arteries is an indication of involvement of the systemic and renal arterioles of similar type and severity." According to Browne (1944) arteriolar spasm can be seen in the arterioles of the retina in pre-eclamptic toxæmia when the blood pressure exceeds 150. Bell (1932) showed that in fatal cases of eclampsia there was a narrowing of all the glomerular capillaries. Herrick and Tillman (1935) found widespread vascular changes in the arteries of the kidneys, spleen, pancreas, suprarenal glands, and liver. Teel *et al.* (1937) found, in addition to œdema and leucocytic infiltration of the myocardium, also minor changes in the small coronary vessels.

Although convincing proof is still lacking of a direct damage to the myocardial vessels in toxæmia of pregnancy, in the light of the above-mentioned clinical and anatomical findings the possibility of structural damage to the small coronary branches cannot be excluded with certainty. There appeared to be no close correlation between the severity of the toxæmic state and the degree of cardiac damage. The duration of the toxæmia may be more important than its severity in producing the cardiac damage.

The true significance of the observations presented in this paper lies in showing that cardiac involvement is not uncommon in toxæmia of pregnancy. We believe that some of the cases of acute ante-partum or post-partum cardiac failure of undetermined ætiology may be instances of toxæmia, even if the recognized signs of the latter condition are not convincingly present at the time of the onset of the cardiac failure; and that some of the cases of vascular collapse known as " obstetric shock " may be instances of true toxæmia. The clinical picture of post-partum vascular collapse in one of our cases (Case 17) was identical with that of so-called " obstetric shock." Most such cases are associated with traumatic delivery and post-partum

loss, and the chief causative factor is blood loss. There remain, however, those infrequent but important cases where collapse occurs with minimal loss after normal labour and delivery, our Case 17 being an example. Such cases may be instances of toxæmia of pregnancy with associated myocardial damage.

Summary and Conclusions

The heart was studied in 19 unselected cases of toxæmia of pregnancy. Clinical and cardiographic examinations were made in all of them, and 9 were also studied radiologically.

Seven patients showed significant cardiac involvement. One developed left ventricular failure, with T wave changes in the cardiogram similar to those seen in anterior myocardial infarction. Two had left ventricular failure with normal cardiographic tracings. Four others showed no clinical evidence of cardiac failure, but their cardiograms showed T wave changes that were interpreted as indicating myocardial damage, and one of these developed post-partum vascular collapse. Six patients showed cardiographic changes of doubtful significance, and in six both the clinical and the cardiographic findings were perfectly normal.

The clinical and cardiographic manifestations were of a transient nature. Cardiac enlargement was found in only one case, and the belief is expressed that gross cardiac enlargement is not a feature of pure " toxæmic " cardiac lesion irrespective of the presence or absence of cardiac failure.

The pathogenesis of the cardiac lesion is discussed, and it is suggested that either direct vascular damage—as in acute glomerulo-nephritis—or primary focal myocardial necrosis, or both, have to be considered.

Cardiac involvement is not an uncommon complication of toxæmia of pregnancy, and some of the unusual types of heart failure occurring in late pregnancy and in the early puerperium, and also some of the cases of post-partum vascular collapse may be instances of toxæmia of pregnancy with associated myocardial damage.

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ABSTRACTS OF CARDIOLOGY

A Study of Abnormal T Waves in Patients presenting No Evidence of Organic Heart Disease. I. STEIN. *J. Lab. clin. Med.*, **31**, 837–849, Aug., 1946.

With wider use of electrocardiographs it is increasingly important that minor deviations should not be taken for evidence of heart disease, and that the limits of the normal should be widely recognized. Stein has studied 4810 soldiers at an Army hospital who were considered free from heart disease. Most were men between 20 and 40. More than 1 per cent (51) showed T wave changes that might be thought pathological; 23 predominantly in CR4 and 28 in the standard limb leads. More than half of these were psychoneurotic, and none had any other evidence of heart disease after full examination, including cardioscopy. Forty-three of 50 patients with T wave changes had normal upright T waves after exercise.

When Graybrel and White first drew attention to the possibility of T II inversion without heart disease it was mainly in patients with neuro-circulatory asthenia, though the importance of posture and a high diaphragm was also stressed. The authors did not think that fear or emotion resulting from the examination was the responsible factor, but rather attributed the changes to autonomic nervous imbalance. They stress the importance of not making a mistaken diagnosis of heart disease.

Maurice Campbell

The Influence of Age on Blood Pressure. A Study of 5,331 White Male Subjects. H. I. RUSSEK, M. M. RATH, B. L. ZOHMAN, and I. MILLER. *Amer. Heart J.*, **32**, 468–479, Oct., 1946.

A statistical analysis of the systolic and diastolic blood pressure readings of 5331 white males between the ages of 40 and 95 years is presented. The subjects were observed in two service hospitals and two institutions for aged people. The gist of the findings is that a systolic blood pressure below " 100 plus the age " is " normal," and a diastolic blood pressure of over 90 mm. Hg. is abnormal at any age.

H. E. Holling

Magnesium Sulfate in Paroxysmal Tachycardia. W. T. ZIMDAHL. *Ann. intern. Med.*, **25**, 531–533, Sept., 1946.

An attack of paroxysmal auricular tachycardia, which responded to intravenous magnesium sulphate, is described. Carotid sinus pressure, ocular pressure, quinidine sulphate (3 gr. (0·2 g.) intravenously every 2 hours for 12 hours), rapid digitalization with lanatocide-C, 0·8 mg. intravenously followed by 0·1 g. of digitalis leaf every 4 hours, and mecholyl (acetyl β-methylcholine chloride) 25 mg. subcutaneously, were all tried without effect. As the patient's condition was so poor it was considered advisable to stop the arrhythmia if possible, and he was given 10 ml. of 25% magnesium sulphate solution intravenously. This, too, had no effect, so 6 hours later he was given 22 ml. of 25% magnesium sulphate solution intravenously and the attack ceased while the needle was still in the vein. This dosage is somewhat higher than that usually recommended of 10 to 20 ml. of 20% solution.

S. Oram

Effect of 1262 F (" Dacorene ") on Recurrent Paroxysmal Tachycardia. R. FROMENT and L. GALLARVADIN. *J. Méd. Lyon*, **27**, 725–726, Oct. 20, 1946.

" Dacorene " (diethyl-aminoethoxy-2-diphenyl chlorhydrate) is a synthetic sympathetic inhibitor said to act predominantly on the heart. The authors report the results of its administration in 2 cases—one of supraventricular paroxysmal tachycardia and one of auricular flutter. [No electrocardiograms are reproduced.] The first patient, a man of 53, had had attacks of tachycardia since the age of 6; after the age of 46 they became more frequent and of longer duration. With quinidine 9 gr. (0·6 g.) thrice daily the frequency of the attacks was reduced, but the drug gave rise to toxic symptoms. The dose was reduced and on the whole the frequency of the attacks continued to diminish, though varying from time to time. Dacorene was combined with the quinidine, and then the two drugs were given alternately. The attacks gradually became less, and of about the same frequency with either drug. The dacorene had no toxic effects. In the second case, that of a man of 64, there were attacks of auricular flutter with 1-to-1 response or 2-to-1 or a higher degree of block. Quinidine was without effect on these paroxysms, but dacorene (150 mg. 4 times daily) suppressed them while the patient was in hospital. He continued this dosage for a month after his discharge and remained free of attacks. Then he took smaller and irregular doses and noted a recurrence of the paroxysms. Indications for its use, dosage, and mode of action have still to be worked out.

S. H. Cookson

The Conducting System of the Vertebrate Heart. F. DAVIES and E. T. B. FRANCIS. *Biological Reviews*, **21**, 173–188, Oct., 1946.

A brief review is given of the most important work on the structures responsible for the initiation and conduction of the impulse to contraction in the vertebrate

heart. The authors conclude that in fish, amphibia, and reptiles the cardiac muscle fibres form a continuum with the same general histological characters in all parts of the heart. Since there is no structural specificity of the muscle fibres, factors other than purely morphological ones must account for the different intrinsic rhythms displayed by the individual heart chambers. They suggest, on the basis of unpublished work, that a differential distribution between auricle and ventricle of certain chemical substances (glycogen, phosphocreatine, and adenosine compounds), known to be concerned with muscular contraction, may have a bearing on this problem.

In birds and mammals, specialized tissue (the nodes, A-V bundle, and Purkinje fibres) has been developed to initiate and conduct the impulse to contraction. The structure and distribution of these specialized fibres are in general the same for birds and mammals. There are, however, certain differences which the authors hold may be related to the different functional requirements of the hearts. Collateral evidence is brought to support the view that the specialized tissues of the avian and mammalian heart are not remnants of more extensive tissues of a similar nature in lower vertebrate hearts, but are new developments associated with the more rapid heart rate in the higher vertebrates.

R. T. Grant

Complete Heart Block in Pregnancy. T. J. QUINTIN. *Canad. med. Ass. J.*, **55**, 600–601, Dec., 1946.

Complete heart block is a rarity among pregnant women, 14 cases only having been recorded up to 1938. The author describes a patient who had two normal pregnancies and confinements. Symptoms were negligible except for slight dyspnœa on exertion during the last 2 months before the second confinement and some giddiness after stooping. Laboratory investigations did not reveal the cause of the heart block. *Braithwaite Rickford*

Prognostic Significance of the Diastolic Blood Pressure in Eclampsia Patients. L. VÁCZY. *Gynaecologia*, **122**, 244–251, Oct., 1946.

It is difficult to decide whether the course of an eclamptic case will be mild or severe. Various investigations, such as estimation of the histamine content of the urine, measurement of capillary pressure in the skin or of muscle tone, and liver function tests, have been suggested in the past but are of little use at the bedside. This paper shows the value of blood pressure readings in prognosis during the acute stage of eclampsia. The systolic, pulse, and diastolic pressure readings in 24 cases are discussed.

No prognostic significance could be attached to the systolic blood pressure. Thus, 12 of the 24 patients had an average systolic blood pressure of over 180 mm. and had only 3 fits, while 12 with an average of 178 mm. had more than 3 fits. Further, 7 women who had only 1 fit had a systolic pressure of over 200 mm. while 6 who had 5 fits had one of less than 200 mm. The pulse pressure was also of no prognostic value. Patients with a diastolic pressure of over 100 mm. generally had more fits than those with a diastolic pressure below 100. There was no absolute connection between the height of the diastolic pressure and the number of fits, but it could be said that when the diastolic pressure was below 100 mm. the prognosis was better than when it was above 100. *Gladys Dodds*

Atherosclerotic Valvular Disease of the Heart. C. T. ASHWORTH. *Arch. Path.*, **42**, 285–298, Sept., 1946.

The author found atherosclerotic valvular disease of the heart recorded in 101 of 500 consecutive necropsies. and himself found changes of some degree in 63% of hearts carefully examined. The lesions were moderate or severe in 7% of the 500 necropsies. The mitral valve was usually the first to be affected, but in most cases both it and the aortic valve were involved. The tricuspid and pulmonary valves always escaped. The earliest lesion was an atheromatous one on the "outflow" surface of the valve—that is, the aortic surface of the aortic valve, and the ventricular surface of the mitral valve. Diffuse thickening or sclerosis followed, often with the deposition of calcareous plaques. The more extreme lesions of the aortic valve caused stenosis and insufficiency. The anterior cusp of the mitral valve was more commonly and more intensely involved than the posterior; calcification, stenosis, and incompetence were all rarer than in the aortic valve. In 10 hearts the annulus fibrosus of the mitral valve was occupied by a more or less complete ring of calcification; two of these cases had had complete heart block.

The frequency and severity of the lesions increased with age, and changes of some degree were nearly always present in subjects over 50 years. Incidence was not related to sex or race, nor was valvular sclerosis related to hypertension. The disease was not often clinically manifest, and only the more severe lesions caused cardiac murmurs. The more extreme degrees of calcification sometimes contributed to death by aortic stenosis or by heart-block due to calcification of the annulus fibrosus of the mitral valve. The degree of valvular atherosclerosis was similar to that in the upper aorta and coronary arteries. The ætiology of the condition would appear to be the same as that of atherosclerosis elsewhere, with the additional factors that the affected parts of the valves are the least cellular and vascular, and the most subject to tension and vibration. *Martin Hynes*

The Relation between Circulation Time and the Amount of the Residual Blood of the Heart. B. GERNANDT and G. NYLIN. *Amer. Heart J.*, **32**, 411–418, Oct., 1946.

The authors have measured the "circulation time," the "heart volume," and the brachial venous pressure in 308 patients with heart disease. In 214 of the patients the heart lesion was compensated and

in 94 it was decompensated, as evidence by œdema, a palpable liver and spleen, and pulmonary congestion.

They find in all cases a significant relation between the heart volume and the circulation time. They also state that " the studies have clearly proved that, above all, the circulation time depends on the amount of residual blood in the heart and only to a slight extent on the degree of decompensation, i.e., of congestion."

Correlation	Number	r±Or
Volume (V/M^2)–circulation time	93	0·37±0·090
Volume (V/M^2)–venous pressure	93	0·37±0·090
Venous pressure–circulation time	94	0·39±0·088

[This last statement does not seem to be borne out by the correlation coefficients given for relative heart volume, circulation time, and degree of decompensation (as measured by the venous pressure) as shown in the table.] *H. E. Holling*

Cardiac Output in Heart Failure. J. R. E. SUAREZ, J. C. FASCIOLO, and A. C. TAQUINI. *Amer. Heart J.*, **32**, 339–356, Sept., 1946.

This is a study of 42 patients with different types of valvular, hypertensive, or coronary heart disease, and of 17 normal subjects. The cardiac patients were graded into 4 classes according to the criteria of the New York Heart Association: (1) patients with no limitation of physical activity; (2) those with slight limitation of physical activity; (3) those with marked limitation; and (4) those who are unable to carry on any physical activity without discomfort. Grollman's acetylene method was used, 4 samples being taken. The results were subjected to statistical analysis; and are shown in the table:

	Normal	Class 1	Class 2	Class 3	Class 4
Cardiac index in litres per sq. metre per minute	2·27 ±0·06	2·35 ±0·19	2·03 ±0·05	1·73 ±0·09	1·58
Arterio-venous oxygen difference in ml. per litre of blood	60·4 ±1·78	62·2 ±6·53	66·9 ±1·85	81·0 ±3·96	91·8
Systolic output in ml. per sq. metre of body surface	35·4 ±0·76	35·3 ±2·81	29·8 ±1·14	23·8 ±1·29	19·3
Pulse rate: Mitral disease	63	63	70	83	98
Other diseases		74	66	71	77

Classes 3 and 4 represent failure.

The authors conclude that there is an inverse correlation between the degree of cardiac failure and the cardiac output, and a direct correlation between the degree of failure and increase in the arterio-venous oxygen difference. Systolic output goes down as failure increases in degree. In mitral cases the pulse rate rises as failure advances, but in other forms of heart disease behaviour of the rate is rather irregular.

James W. Brown

Myocardial Lesions due to Starvation. R. FORSTER. *Cardiologia.*, **10**, 369–378, 1946.

This paper describes the clinical and post-mortem changes in 31 cases of starvation from German concentration camps. The most frequent electrocardiographic finding was a reduction in amplitude of the deflections, particularly of the T wave. At necropsy the most frequent cardiac change found was fatty degeneration of the myocardium. In these cases recognizable vitamin deficiencies were seldom seen, though infections and pre-existing cardiac abnormalities were frequent. The mechanism of the changes seen is discussed. *H. E. Holling*

The T Wave of the Precordial Electrocardiogram at Different Age Levels. R. M. SUAREZ and R. M. SUAREZ, JR. *Amer. Heart J.*, **32**, 480–493, Oct., 1946.

Inverted T waves occur in the præcordial electrocardiograms of normal subjects up to 15 years of age. The present observations were made to determine the incidence of these findings in various age groups in 161 healthy Puerto Ricans, aged 5 to 46 years. With the exploring electrode paired with the arm and leg leads through a central terminal, records were taken from the six classical chest positions (C.V.1 to C.V.6). In the youngest subjects up to 12 years old, inverted or diphasic T waves were found as far laterally as position 5, in subjects 12 to 18 years of age as far as position 4, and in adults as far as position 3. The results suggest that, irrespective of age or sex, a negative T wave in C.V.6 may be regarded as abnormal while the same finding in C.V.1 may be normal. Negative T waves in C.V.4 or C.V.5 are probably abnormal over 12 years of age.

W. J. H. Butterfield

The Heart in Rheumatoid Arthritis. A. S. ROGEN. *Brit. med. J.*, **1**, 87–88, Jan. 18, 1947.

The author reviews recent work on the ætiological relationships between rheumatic fever and rheumatoid arthritis, with special reference to the cardiovascular system in 33 consecutive cases of rheumatoid arthritis, 22 of which were females. Careful search was made for evidence of mitral stenosis but none was found. In 1 case only, a woman of 68, was there a loud apical systolic bruit which was considered to be organic; in 8 cases there was a functional murmur. The electrocardiograms of 29 patients showed no changes that could be held to be suggestive of rheumatic fever, though in some cases there were T wave

changes corresponding in all probability to the state of arterial degeneration occurring in old people, who formed the majority of the patients in this series. No macroscopical or histological changes of rheumatic fever were seen in the 1 case that came to necropsy.

These results are at variance with the reports of some, but not all, workers, and serve to emphasize the limited value of comparisons between the clinical manifestations of rheumatic fever and rheumatoid arthritis in the present state of our knowledge of the rheumatic diseases. *J. W. Brown*

A Refractory Case of Subacute Bacterial Endocarditis due to *Veillonella gazogenes* clinically Arrested by a combination of Penicillin, Sodium para-Amino-hippurate and Heparin. L. LOEWE, P. ROSENBLATT, and E. ALTUREWERBER. *Amer. Heart J.*, **32**, 327–338, Sept., 1946.

The unique case is described of a 35-year-old man who suffered from subacute bacterial endocarditis due to *Veillonella gazogenes*, a Gram-negative anærobic coccus. During a year of treatment he received about 467,000,000 units of penicillin, and, at the end of that time, although his blood culture was still positive and his subacute endocarditis active, he was felt not to have deteriorated much. *In vitro* tests showed bacteriostasis at 10 units of penicillin per ml., and that 30 units per ml. were required for a complete bactericidal effect. Previous studies had shown that a blood level of 1 unit per ml. could be expected for each million units of penicillin administered daily. Thus to reach the desired level 30,000,000 units a day was necessary. It was therefore decided to use *p*-aminohippuric acid as an enhancing agent. Treatment was accordingly started by the intravenous route with the daily administration of 10,000,000 units of penicillin dissolved in 2 litres of 12 per cent sodium *p*-aminohippurate solution to which was added 50 mg. of heparin. The heparin was used to prevent thrombophlebitis at the site of injection. This mixture produced prompt results, and within 3 days the temperature became normal, and has remained so for 6 months. The treatment was continued for 13 days, so that the patient received a total of 130,000,000 units of penicillin. *James W. Brown*

Acute Myocardial Infarction in Men Below Forty. F. STEIGMANN and F. CLASSNER. *Mil. Surg.*, **99**, 177–181, Sept., 1946.

The authors describe acute myocardial infarction in 3 patients, aged 28, 32, and 34, in a naval hospital. Observations during the war make it necessary to adjust ideas as to incidence and causative factors. Only recently have reports appeared of patients below 40 suffering from coronary thrombosis—a diagnosis which now has to be considered in patients with severe substernal or præcordial pain, be their age 20 or 60 War experience emphasizes effort as precipitating an attack. Without implying that this condition cannot occur while at rest in bed, it is noted that in one series 50 per cent followed effort, and only 10 per cent occurred during sleep.

Kahn tests were negative in all 3 patients. The pneumonitis in the first 2 patients was regarded as contributory. Effort played a part in all 3. Electrocardiographic changes are delayed, showing the importance of serial examinations.

Failure to recognize effort as a cause, and the possibility of the occurrence of the disease in younger people, might have catastrophic effects. The authors consider that arteriosclerosis of the coronaries may occur in young individuals and that effort, cold, and over-eating may bring on acute myocardial infarction with or without associated thrombosis of the coronary vessels. *W. N. Pickles*

Bacterial Endocarditis of the Tricuspid Valve. L. KAROTKIN and P. MARCUSE. *South med. J.*, **39**, 769–774, Oct., 1946.

The authors draw attention to the difficulty of diagnosing bacterial endocarditis involving only the right side of the heart; signs of organic heart disease are often lacking, the blood culture usually remains negative, and systemic embolism fails to appear unless tissue breakdown occurs in the lungs. They report 3 cases of bacterial endocarditis of the tricuspid valve, giving necropsy findings in each case. Case 1 had a tricuspid valve already damaged by rheumatism; early blood culture was negative, but later pneumococcus Type VII was grown from venous blood. In Case 2 the endocarditis complicated lobar pneumonia, and the sputum contained Type VII pneumococcus; blood culture was not performed. In Case 3 the valvular lesion occurred in the course of a *Staphylococcus aureus* septicæmia, and blood culture was repeatedly positive. Acute bacterial endocarditis of the tricuspid valve alone is rare, and subacute bacterial endocarditis of this valve is even more rare. On the other hand, involvement of the tricuspid valve in addition to other valves is " perhaps not quite so rare as is commonly believed." *D. Black*

Study of the Electrocardiogram in Auriculo-Ventricular Block. (Étude de l'électrocardiogramme dans le bloc atrio-ventriculaire.) G. FATZER. *Cardiologia, Basel*, **10**, 305–368, 1946.

Forty-four cases of total A–V block were studied (19 men, 25 women). Arteriosclerosis and rheumatic myocarditis were the main causes. Arteriosclerosis is more liable to produce intermittent block than myocarditis. The prognosis of A–V block depends on the condition of the myocardium, the frequency of Adams-Stokes attacks which carry a bad prognosis, the presence of bundle-branch block, and the length of the Q–T interval. Sinus arrhythmia, blood pressure, hæmoglobin values, cardiac enlargement (observed in most cases), and decompensation (in 50 per cent of the cases) were studied in detail. *H. E. Holling*

Coronary Sinus Rhythm. D. SCHERF and R. HARRIS. *Amer. Heart J.*, **32**, 443–456, Oct., 1946.

In the course of 23,610 routine electrocardiac examinations 31 cases of coronary sinus rhythm were diagnosed on the criteria of low positive or absent P waves in lead I, deep, inverted, and usually peaked P waves in leads II and III, and a normal or slightly shortened P–R interval. These changes were previously observed by Scherf in dogs after warming the coronary sinus *in situ*. The cases were evenly distributed between the sexes, and the majority of patients showed evidence of heart disease. The rhythm was very labile and changed spontaneously or after exercise, amyl nitrite inhalations, or carotid sinus pressure. As the authors point out, it should be noted that, in our present state of knowledge, it is not possible to differentiate between rhythms originating in the region of the coronary sinus and in the upper part of the auriculo-ventricular node. *W. J. H. Butterfield*

Abnormalities of the Respiratory Pattern in Patients with Cardiac Dyspnea. H. E. HEYER. *Amer. Heart J.*, **32**, 457–467, Oct., 1946.

The movements of the chest wall during respiration were recorded from a Marey pneumograph on to a kymograph drum. In this way the "respiratory pattern" was studied in 5 normal subjects, 11 cases of cardiac disease with clinical pulmonary congestion, and in 2 cases of allergic asthma during the attacks. In the last two groups of subjects the tracings confirmed the presence of a prolongation of expiration and showed a terminal slowing in this phase. After exercise these cases did not show the relative shortening of expiration, as compared with inspiration, which was seen in the normal subjects. However, after receiving 0·5 g. aminophylline intravenously, 5 out of 6 cases of pulmonary congestion and both cases of asthma showed faster breathing presumed to be of central origin, with greatly increased vital capacity and shortening of the expiratory phase without terminal slowing, which in the author's opinion is due to the relaxation of bronchospasm.
W. J. H. Butterfield

Diet Low in Salt (Sodium) in Congestive Heart Failure. E. O. WHEELER, W. C. BRIDGES, and P. D. WHITE. *J. Amer. med. Ass.*, **133**, 16–20, Jan. 4, 1947.

One of the most important changes associated with heart failure is an increase in volume of the circulating blood. This tends to be particularly distributed in the venous circulation and seems to be associated with a rise in venous pressure. There is no doubt that in many cases of heart failure retention of sodium by the kidney occurs quite early. This is associated with an increase in the patient's weight, probably due to increase in the extracellular tissue fluid. There is *pari passu* with the retention of sodium a retention of water. This state of affairs soon leads to the development of œdema. It would appear that œdema can be precipitated by feeding sodium chloride to patients who have a mild degree of heart failure.

The treatment of œdema has been developed with particular attention to the reduction of sodium in the diet. If a diet low in sodium is given, it is possible to allow a fluid intake dictated by the patient's taste. The average diet, without salt added at table, contains about 4 to 7 g. of sodium chloride; without salt added in cooking, it contains 3 to 4 g.; a low-sodium diet contains 1·5 to 2 g. of sodium chloride. No drugs containing sodium should be given. On this diet, with the help of occasional mercurial diuretics, or even without them, a patient can become free from œdema and remain so. The disadvantage is in the tasteless food. *Terence East*

Some Observations on the Pathogenesis of Edema in Cardiac Failure. F. REICHSMAN and H. GRANT. *Amer. Heart J.*, **32**, 438–442, Oct., 1946.

Observations were made on 3 patients with rheumatic heart disease and auricular fibrillation, treated with digitalis. All 3 patients had had repeated attacks of cardiac failure, in 2 of them associated with œdema. When in hospital on a diet containing about 3 to 4 g. of sodium chloride the digitalis was withdrawn, and the venous pressure (measured directly) in these patients rose before there was formation of œdema.
E. B. Reeve

The Rationale for the Treatment of Angina Pectoris by Irradiation of the Adrenal Glands. W. C. FISHER and R. L. MCMILLAN. *N. C. med. J.*, **7**, 547–550, Oct., 1946.

Experimental evidence from the literature is selected to lend support to the view that angina pectoris is due to discharges of adrenaline, which increase the cardiac demand for oxygen, coupled with inability of atherosclerotic coronary arteries to dilate proportionately. Thus the heart of a dog acted on by adrenaline may consume four times the normal amount of oxygen. The four most common precipitating causes of angina —effort, emotion, over-eating, and cold—have been shown to provoke an adrenaline discharge. A subcutaneous injection of 0·5 to 1 mg. of adrenaline is known to induce an attack of angina pectoris in 90 per cent of subjects afflicted with the disease. The activity of the adrenal secretory mechanism may be reduced by irradiation of the adrenal glands. Patients so treated, who show a reduction in the severity or frequency of attacks, no longer respond to the precipitating factors mentioned above by an adrenal discharge. Those who do not improve continue to show the response. *Paul Wood*

Disadvantages of Thiouracil Treatment of Angina Pectoris. J. R. DIPALMER and J. J. MAGOVERN. *Amer. Heart J.*, **32**, 494–503, Oct., 1946.

Eight patients with angina pectoris who had been under observation for several years were given thiouracil (usually 0·6 g. daily) for periods ranging

from 3 weeks to 14 months. The effects on their anginal pain, exercise tolerance, and basal metabolic rate were studied. Difficulty was experienced in lowering the basal metabolic rate of the optimum level of −10 to −20 per cent, at which levels the anginal pain was less severe; below these levels the patients became too myxœdematous. The authors believe that there is a tendency for water retention to occur as the metabolism is lowered, so that pulmonary œdema and increased dyspnœa appear. Two patients developed toxic skin rashes. Four of them benefited from the thiouracil, but in only 2 of these was the improvement marked. Both of these had a raised basal metabolic rate before treatment, a finding which is considered the only indication for use of the drug other than as a therapeutic test in the selection for thyroidectomy of patients with angina pectoris.

B. McArdle

The Treatment of Angina Pectoris by Irradiation of the Adrenal Glands; Clinical Experience. R. L. McMillan and J. P. Rousseau. *N. C. med. J.*, **7**, 550–553, Oct., 1946.

The adrenal glands of 23 patients with severe angina pectoris were irradiated, each adrenal area receiving 600 r. in three divided doses over a week. Thirteen patients were greatly relieved, 4 moderately so, 3 slightly, and 3 not at all. The period of observation was 2 to 12 months. Two of the patients who most benefited died suddenly during this time, and a third died from probable myocardial infarction. Blood pressure readings did not change significantly in the males, but showed an average drop of 23/22 mm. in the females. On the whole, patients seemed less emotional after treatment. The most severe cases, and those in which attacks were especially provoked by emotion, did best. The subsequent incidence of myocardial infarction and the life expectancy are assumed to remain unaltered. *Paul Wood*

Cardiac Muscle. Further Studies; Investigation of Chemical Changes in Myocardial Insufficiency with Special Reference to Adenosinetriphosphate. G. H. Mangun and V. C. Myers. *Arch. intern. Med.*, **78**, 441–446, Oct., 1946.

The creatine, the total phosphorus and acid-soluble phosphorus, and possibly the potassium content of a failing heart muscle are usually decreased. In the dog with myocardial insufficiency due to induced aortic incompetence, Mangun and Roberts had noted a marked decrease in the adenosine-triphosphate and phosphocreatine content of the left ventricle. The present authors use a new method for the estimation of total acid-soluble purines and of oxypurines, which involves hydrolysis of purine compounds, deamination with nitrous acid, precipitation with copper bisulphite, and estimation of the nitrogen content of the precipitate. They claim that the acid-extractable purine content of the left ventricle, calculated as adenine, is decreased in myocardial insufficiency. Lowered concentrations of purine were also observed in the myocardium of the right ventricle in some, but not in all, cases of pneumonia. *Henry Cohen*

Disseminated Parenchymatous Ossification in the Lungs in Association with Mitral Stenosis. A. Elkeles and L. E. Glynn. *J. Path. Bact.*, **58**, 517–522, Sept., 1946.

The case described is of a man of 32 years who died of congestive heart failure due to mitral stenosis; before death X rays showed numerous dense miliary shadows on both sides, the typical cardiac outline of mitral stenosis was also present. At necropsy the lungs showed brown induration and there were 2 small infarcts. Microscopically the radio-opaque nodules were found to be true bone, filling groups of alveoli and extending into the alveolar ducts; there were also small amorphous calcareous fragments lying in alveoli and occasionally capping the bony structures. Sections stained for elastic tissue showed the remains of the interalveolar structure contained within the bone. The other lung lesion of interest was an active rheumatic inflammation of arteries: intimal proliferation, medial fibrinoid necrosis, and adventitial histiocytic infiltration; there was also chronic passive congestion and interstitial fibrosis. The heart showed a severe degree of mitral stenosis and there was also evidence of aortic incompetence.

W. S. Killpack

Miliary Appearances and Manifestations of Pulmonary Stasis in Mitral Disease. M. Leblanc. *Arch. Mal. Cœur*, **39**, 69–74, March–April, 1946.

The case is reported of a man who was known to have had rheumatic carditis since the age of 20 and some dyspnœa since the age of 41. There were signs of mitral stenosis, auricular fibrillation, and systemic congestion. His blood pressure was 165/115 mm. Chest skiagrams showed, in addition to the heart of mitral stenosis, a generalized marbling of the lung fields, most marked in the mid-zones. This appeared to be due to two elements—small cavities and miliary nodules—which together suggested pulmonary tuberculosis. The sputum was negative for tubercle bacilli. Treatment for cardiac failure was given, and after 2 months symptoms were relieved, but the X-ray appearance of the lungs was unchanged apart from the absorption of a pleural effusion. The miliary pulmonary nodules which are a rare feature of mitral stenosis are said to be composed of "heart-failure cells" and blood pigment derived from extravasated red cells. *Harold Cookson*